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(71) Applicants:

• Novartis AG

4058 Basel (CH)

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• Novartis-Erfindungen Verwaltungsgesellschaft
m.b.H.
1230 Wien (AT)
Designated Contracting States:
AT

(72) Inventors:

• Chabrecek, Peter

4125 Riehen (CH)

• Lohmann, Dieter

4141 Münchenstein (CH)

(74) Representative: Becker, Konrad

Novartis AG,

Corporate Intellectual Property,

Patent & Trademark Department

4002 Basel (CH)

(54) Process for coating a material surface

(57) The invention relates to a process for coating a material surface, comprising the steps of:

(a) providing the material surface with polymer brushes comprising polymerization initiator radicals; and

(b) graft polymerizing one or more different ethylenically unsaturated hydrophilic monomers or macromonomers onto the polymerization initiator-modified polymer brushes.

The coated articles that are obtainable by the process of the invention have desirable characteristics regarding adherence to the substrate, durability, hydrophilicity, wettability, biocompatibility and permeability and are thus useful for the manufacture of biomedical articles such as ophthalmic devices.

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Description

[0001] The present invention relates to a process for the manufacture of coated articles wherein the coating comprises a polymer having desirable characteristics regarding adherence to the substrate, durability, hydrophilicity, wettability, biocompatibility and permeability. More particular, the present invention relates to a process for the modification of the surface of an article, such as a biomedical material or article, especially a contact lens including an extended-wear contact lens wherein the articles are at least partly coated with a polymer having a "bottle-brush" type structure composed of tethered "hairy" chains.

[0002] A variety of different types of processes for preparing polymeric coatings on a substrate have been disclosed in the prior art. For example, U.S. patent No. 5,527,925 describes functionalized photoinitiators and also organic substrates such as contact lenses containing said photoinitiators covalently bound to their surface. In one embodiment of said disclosure, the so modified surface of the contact lens is further coated with a photopolymerizable ethylenically unsaturated monomer which is then polymerized by irradiation thus forming a novel substrate surface. With this method, however, it is not always possible to obtain the desired coating characteristics, for example wettability characteristics which are necessary for the surface of biomedical devices including contact lenses. In particular, the ability of the known materials to attract and stabilize a continuous layer of an aqueous solution, e.g. human body fluids such as tears or mucus layers, for a prolonged period of time which is an important feature for many biomedical applications is not yet satisfactory.

[0003] Surprisingly, it now has been found that articles, particularly biomedical devices such as contact lenses, with an improved wettability, water-retention ability and biocompatibility are obtained by first of all providing the article surface with a brush-type primary polymer coating comprising polymerization initiator radicals; and then grafting one or more different ethylenically unsaturated hydrophilic monomers onto the initiator-modified polymer chains that make up the brush structure.

[0004] The present invention therefore in one aspect relates to a process for coating a material surface, comprising the steps of:

- (a) providing the material surface with polymer brushes comprising polymerization initiator radicals; and
- (b) graft polymerizing one or more different ethylenically unsaturated hydrophilic monomers or macromonomers onto the polymerization initiator-modified polymer brushes.

[0005] Examples of materials that may be coated according to the process of the invention are quartz, ceramics, glasses, silicate minerals, silica gels, metals, metal oxides, carbon materials such as graphite or glassy carbon, natural or synthetic organic polymers, or laminates, composites or blends of said materials, in particular natural or synthetic organic polymers which are known in large number. Some examples of polymers are polyaddition and polycondensation polymers (polyurethanes, epoxy resins, polyethers, polyesters, polyamides and polyamides); vinyl polymers (polyacrylates, polymethacrylates, polystyrene, polyethylene and halogenated derivatives thereof, polyvinyl acetate and polyacrylonitrile); elastomers (silicones, polybutadiene and polyisoprene); or modified or unmodified biopolymers (collagen, cellulose, chitosan and the like).

[0006] A preferred group of materials to be coated are those being conventionally used for the manufacture of biomedical devices, e.g. contact lenses, in particular contact lenses for extended wear, which are not hydrophilic per se. Such materials are known to the skilled artisan and may comprise for example polysiloxanes, perfluoropolyethers, fluorinated poly(meth)acrylates or equivalent fluorinated polymers derived e.g. from other polymerizable carboxylic acids, polyalkyl (meth)acrylates or equivalent alkylester polymers derived from other polymerizable carboxylic acids, or fluorinated polyolefines, such as fluorinated ethylene propylene, or tetrafluoroethylene, preferably in combination with specific dioxols, such as perfluoro-2,2-dimethyl-1,3-dioxol. Examples of suitable bulk materials are e.g. Lotrafilcon A, Neofcon, Pasifocon, Telefocon, Silafocon, Fluorsilfocon, Paflufocon, Silafocon, Elastofilcon, Fluorofocon or Teflon AF materials, such as Teflon AF 1600 or Teflon AF 2400 which are copolymers of about 63 to 73 mol % of perfluoro-2,2-dimethyl-1,3-dioxol and about 37 to 27 mol % of tetrafluoroethylene, or of about 80 to 90 mol % of perfluoro-2,2-dimethyl-1,3-dioxol and about 20 to 10 mol % of tetrafluoroethylene.

[0007] Another preferred group of materials to be coated are those being conventionally used for the manufacture of biomedical devices, e.g. contact lenses, which are hydrophilic per se, since reactive groups, e.g. carboxy, carbamoyl, sulfate, sulfonate, phosphate, amine, ammonium or hydroxy groups, are inherently present in the material and therefore also at the surface of a biomedical device manufactured therefrom. Such materials are known to the skilled artisan and comprise for example polyhydroxyethyl acrylate, polyhydroxyethyl methacrylate (HEMA), polyvinyl pyrrolidone (PVP), polyacrylic acid, polymethacrylic acid, polyacrylamide, polydimethylacrylamide (DMA), polyvinyl alcohol or copolymers for example from two or more monomers from the group hydroxyethyl acrylate, hydroxyethyl methacrylate, N-vinyl pyrrolidone, acrylic acid, methacrylic acid, acrylamide, dimethyl acrylamide, vinyl alcohol and the like. Typical examples are e.g. Polymacon, Tefilcon, Methafilcon, Deltafilcon, Bufilcon, Phemfilcon, Ocufilcon, Focofilcon, Etafilcon, Hefilcon,

Vifilcon, Tetrafilcon, Perfilcon, Droxifilcon, Dimefilcon, Isofilcon, Mafilcon, Nafilcon or Atlafilcon.

[0008] Still another group of preferred materials to be coated are amphiphilic segmented copolymers comprising at least one hydrophobic segment and at least one hydrophilic segment which are linked through a bond or a bridge member. Examples are silicone hydrogels, for example those disclosed in PCT applications WO 96/31792 and WO 97/49740 which are herewith incorporated by reference.

[0009] The material to be coated may also be any blood-contacting material conventionally used for the manufacture of renal dialysis membranes, blood storage bags, pacemaker leads or vascular grafts. For example, the material to be modified on its surface may be a polyurethane, polydimethylsiloxane, polytetrafluoroethylene, polyvinylchloride, Dacron™ or a composite made therefrom.

[0010] Moreover, the material to be coated may also be an inorganic or metallic base material with or without suitable reactive groups, e.g. ceramic, quartz, or metals, such as silicon or gold, or other polymeric or non-polymeric substrates. E.g. for implantable biomedical applications, ceramics or carbohydrate containing materials such as polysaccharides are very useful. In addition, e.g. for biosensor purposes, dextran coated base materials are expected to reduce nonspecific binding effects if the structure of the coating is well controlled. Biosensors may require polysaccharides on gold, quartz, or other non-polymeric substrates.

[0011] The form of the material to be coated may vary within wide limits. Examples are particles, granules, capsules, fibres, tubes, films or membranes, preferably moldings of all kinds such as ophthalmic moldings, in particular contact lenses.

[0012] The polymer brushes according to step (a) of the process of the invention may be provided, for example, by

- 20 (a1) covalently binding polymerization initiator radicals to the surface;
- (a2) graft polymerizing a vinyl monomer carrying a reactive group onto the initiator-modified material surface and thereby providing the surface with polymer brushes comprising reactive groups; and
- 25 (a3) reacting the reactive groups of the polymer brushes with a polymerization initiator having a functional group that is coreactive with the reactive groups of the polymer brushes.

[0013] According to this embodiment of the invention, in the initial state, the material to be coated carries initiator moieties for radical polymerization covalently bound to its surface. According to a preferred embodiment of the invention, the initiator moieties are covalently bound to the surface of the material to be modified on its surface via reaction

30 of a functional group of the material surface with a reactive group of the initiator molecule.

[0014] Suitable functional groups may be inherently (a priori) present at the surface of the material to be modified on its surface. If substrates contain too few or no reactive groups, the material surface can be modified by methods known per se, for example plasma chemical methods (see, for example, WO 94/06485), or conventional functionalization with groups such as -OH, -NH₂ or -CO₂H produced. Suitable functional groups may be selected from a wide variety

35 of groups well known to the skilled artisan. Typical examples are e.g. hydroxy groups, amino groups, carboxy groups,

carbonyl groups, aldehyde groups, sulfonic acid groups, sulfonyl chloride groups, isocyanato groups, carboxy anhydride

groups, lactone groups, azlactone groups, epoxy groups and groups being replaceable by amino or hydroxy groups,

such as halo groups, or mixtures thereof. Amino groups and hydroxy groups are preferred.

[0015] Polymerization initiators bound on the surface of the material to be coated are typically those that are initiating

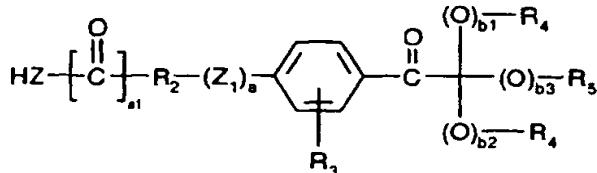
40 a radical polymerization of ethylenically unsaturated compounds. The radical polymerization may be induced thermally, or preferably by irradiation.

[0016] Suitable thermal polymerization initiators are known to the skilled artisan and comprise for example peroxides, hydroperoxides, azo-bis(alkyl- or cycloalkylnitriles), persulfates, percarbonates or mixtures thereof. Examples are benzoylperoxide, tert.-butyl peroxide, di-tert.-butyl-diperoxyphthalate, tert.-butyl hydroperoxide, azo-bis(isobutyronitrile), 1,1'-azo-bis (1-cyclohexanecarbonitrile), 2,2'-azo-bis(2,4-dimethylvaleronitrile), 4,4'-azo-bis(4-cyano-valeric acid, 4,4'-azo-bis(4-cyano-n-pentanol) and the like. The thermal initiators may be linked to the surface of the bulk material by methods known per se, for example as disclosed in EP-A-0378511. Initiators for the thermal polymerization are particularly functional initiators having an initiator part such as a peroxide, hydroperoxide, persulfate or azo group and in addition a functional group that is coreactive with functional groups of the substrate, particularly with -OH, -SH, -NH₂, epoxy, carboxy anhydride, alkylamino,-COOH or isocyanato groups. Suitable functional groups that are coreactive with the surface of the bulk material are for example a carboxy, hydroxy, epoxy or isocyanato group. A particular preferred group of thermal initiators are azo-bis(C₂-C₁₂-alkane carboxylic acids) or azo-bis(C₂-C₁₂-alkanols) wherein the alkane moiety in each case may be further substituted, for example, by cyano.

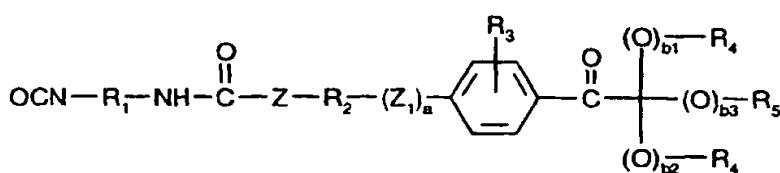
[0017] Initiators for the radiation-induced polymerization are particularly functional photoinitiators having a photoinitiator part and in addition a functional group that is coreactive with functional groups of the substrate, particularly with -OH, -SH, -NH₂, epoxy, carboxy anhydride, alkylamino,-COOH or isocyanato groups. The photoinitiator part may belong to different types, for example to the thioxanthone type and preferably to the benzoin type. Suitable functional groups that are coreactive with the surface of the bulk material are for example a carboxy, hydroxy, epoxy or isocyanato group.

[0018] Preferred polymerization initiators for use in the present invention are the photoinitiators of formulae (I) and (Ia) as disclosed in US patent No. 5,527,925, those of the formula (I) as disclosed in PCT application WO 96/20919, or those of formulae II and III including formulae IIa-IIy and IIIg as disclosed in EP-A-0281941, particularly formulae IIb, III, IIIm, IIIn, IIp, IIr, IIIs, IIx and IIIg therein. The respective portion of said three documents including the definitions and preferences given for the variables in said formulae are herewith included by reference.

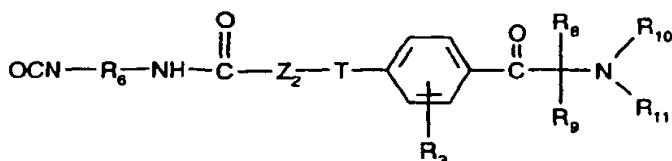
[0019] The polymerization initiator moieties are preferably derived from a functional photoinitiator of the formula



(1a),



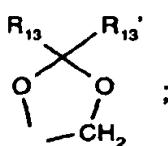
(1b), or



(1c),

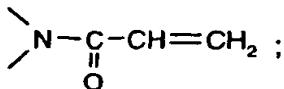
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wherein Z is bivalent -O-, -NH- or -NR₁₂-; Z₁ is -O-, -O-(O)C-, -C(O)-O- or -O-C(O)-O-; R₃ is H, C₁-C₁₂-alkyl, C₁-C₁₂-alkoxy or N-C₁-C₁₂-alkylamino; R₄ and R₅ are each independently of the other H, linear or branched C₁-C₈-alkyl, C₁-C₈-hydroxyalkyl or C₆-C₁₀-aryl, or the groups R₄-(O)_{b1}- and R₄-(O)_{b2}- together are -(CH₂)_c- wherein c is an integer from 3 to 5, or the groups R₄-(O)_{b1}-, R₄-(O)_{b2}- and R₅-(O)_{b3}- together are a radical of the formula



40

45 R₂ is a direct bond or linear or branched C₁-C₈-alkylene that is unsubstituted or substituted by -OH and/or is uninterrupted or interrupted by one or more groups -O-, -O-C(O)- or -O-C(O)-O-; R₁ is branched C₃-C₁₈-alkylene, unsubstituted or C₁-C₄-alkyl- or C₁-C₄-alkoxy-substituted C₆-C₁₀-arylene, or unsubstituted or C₁-C₄-alkyl- or C₁-C₄-alkoxy-substituted C₇-C₁₈-aralkylene, unsubstituted or C₁-C₄-alkyl- or C₁-C₄-alkoxy-substituted C₃-C₈-cycloalkylene, unsubstituted or C₁-C₄-alkyl- or C₁-C₄-alkoxy-substituted C₃-C₈-cycloalkylene-C_yH_{2y}- or unsubstituted or C₁-C₄-alkyl- or C₁-C₄-alkoxy-substituted -C_yH_{2y}-(C₃-C₈-cycloalkylene)-C_yH_{2y}- wherein y is an integer from 1 to 6; R₆ independently has the same definitions as R₁ or is linear C₃-C₁₈-alkylene; R₁₂ is linear or branched C₁-C₆-alkyl; T is bivalent -O-, -NH-, -S-, C₁-C₈-alkylene or



5 Z_2 is a direct bond or $-O-(CH_2)_d$ wherein d is an integer from 1 to 6 and the terminal CH_2 group of which is linked to the adjacent T in formula (10c); R_8 is linear or branched C_1-C_8 -alkyl, C_2-C_8 -alkenyl or C_6-C_{10} -aryl- C_1-C_8 -alkyl; R_9 independently of R_8 has the same definitions as R_8 or is C_6-C_{10} -aryl, or R_8 and R_9 together are $-(CH_2)_e$ wherein e is an integer from 2 to 6; R_{10} and R_{11} are each independently of the other linear or branched C_1-C_8 -alkyl that may be substituted by C_1-C_4 -alkoxy, or C_6-C_{10} -aryl- C_1-C_8 -alkyl or C_2-C_8 -alkenyl; or R_{10} and R_{11} together are $-(CH_2)_{f1}-Z_3-(CH_2)_{f2}$ wherein Z_3 is a direct bond, $-O$, $-S$ or $-NR_7$, and R_7 is H or C_1-C_8 -alkyl and $f1$ and $f2$ are each independently of the other an integer from 2 to 4; R_{13} and $R_{13'}$ are each independently of the other H, C_1-C_8 -alkyl, C_3-C_8 -cycloalkyl, benzyl or phenyl; and a, a_1 , b_1 , b_2 and b_3 are each independently of the other 0 or 1; subject to the provisos that b_1 and b_2 are each 0 when R_{15} is H; that the total of $(b_1+b_2+b_3)$ is not exceeding 2; and that a is 0 when R_{12} is a direct bond.

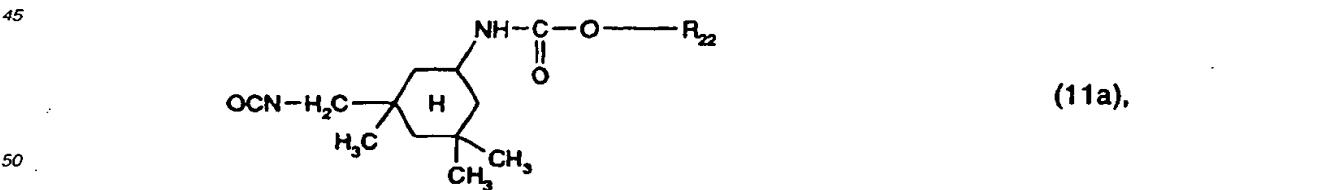
10 [0020] A preferred sub-group of compounds of formula (1a) or (1b) comprises those wherein, b_1 and b_2 are each 0; Z and Z_1 are each bivalent $-O$; b_3 is 0 or 1; R_4 is C_1-C_4 -alkyl or phenyl, or both groups R_4 together are tetramethylene or pentamethylene; R_5 is C_1-C_4 -alkyl or H, R_3 is hydrogen; a and a_1 are each independently 0 or 1; R_2 is linear or branched C_2-C_4 -alkylene, or is a direct bond, in which case a is 0; R_1 is branched C_5-C_{10} -alkylene, phenylene or phe-
15 nylene substituted by from 1 to 3 methyl groups, benzylene or benzylene substituted by from 1 to 3 methyl groups, cyclohexylene or cyclohexylene substituted by from 1 to 3 methyl groups, cyclohexyl- C_yH_{2y} - or $-C_yH_{2y}$ -cyclohexyl- C_yH_{2y} - or cyclohexyl- C_yH_{2y} - or $-C_yH_{2y}$ -cyclohexyl- C_yH_{2y} - substituted by from 1 to 3 methyl groups; and y is 1 or 2.

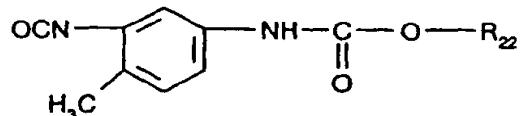
15 [0021] An especially preferred sub-group of compounds of formula (1a) or (1b) comprises those wherein, b_1 and b_2 are each 0, Z and Z_1 are each bivalent $-O$, b_3 is 0 or 1; R_4 is methyl or phenyl, or both groups R_4 together are pentamethylene; R_5 is methyl or H; R_3 is hydrogen; a is 1 and R_2 is ethylene, or a is 0 and R_2 is a direct bond; a_1 is 0 or 1; and R_1 is branched C_6-C_{10} -alkylene, phenylene or phenylene substituted by from 1 to 3 methyl groups, benzylene or benzylene substituted by from 1 to 3 methyl groups, cyclohexylene or cyclohexylene substituted by from 1 to 3 methyl groups, cyclohexyl- CH_2 - or cyclohexyl- CH_2 - substituted by from 1 to 3 methyl groups.

20 [0022] A preferred sub-group of compounds of formula (1c) comprises those wherein T is bivalent $-O$, $-NH$, $-S$ or $-(CH_2)_y$ wherein y is an integer from 1 to 6; Z_2 is a direct bond or $-O-(CH_2)_y$ wherein y is an integer from 1 to 6 and the terminal CH_2 group of which is linked to the adjacent T in formula (10c); R_3 is H, C_1-C_{12} -alkyl or C_1-C_{12} -alkoxy; R_8 is linear C_1-C_8 -alkyl, C_2-C_8 -alkenyl or C_6-C_{10} -aryl- C_1-C_8 -alkyl; R_9 independently of R_8 has the same definitions as R_8 or is C_6-C_{10} -aryl, or R_8 and R_9 together are $-(CH_2)_e$ wherein e is an integer from 2 to 6; R_{10} and R_{11} are each independently of the other linear or branched C_1-C_8 -alkyl that may be substituted by C_1-C_4 -alkoxy, or C_6-C_{10} -aryl- C_1-C_8 -alkyl or C_2-C_8 -alkenyl; or R_{10} and R_{11} together are $-(CH_2)_{f1}-Z_3-(CH_2)_{f2}$ wherein Z_3 is a direct bond, $-O$, $-S$ or $-NR_7$, and R_7 is H or C_1-C_8 -alkyl and $f1$ and $f2$ are each independently of the other an integer from 2 to 4; and R_6 is branched C_6-C_{10} -alkylene, phenylene or phenylene substituted by from 1 to 3 methyl groups, cyclohexylene or cyclohexylene substituted by from 1 to 3 methyl groups, cyclohexyl- CH_2 - or cyclohexyl- CH_2 - substituted by from 1 to 3 methyl groups.

25 [0023] An especially preferred sub-group of compounds of formula (1c) comprises those wherein T is bivalent $-O$; Z_2 is $-O-(CH_2)_y$ wherein y is an integer from 1 to 4 and the terminal CH_2 group of which is linked to the adjacent T in formula (10c); R_3 is H; R_8 is methyl, allyl, tolylmethyl or benzyl, R_9 is methyl, ethyl, benzyl or phenyl, or R_8 and R_9 together are pentamethylene, R_{10} and R_{11} are each independently of the other C_1-C_4 -alkyl or R_{10} and R_{11} together are $-CH_2CH_2OCH_2CH_2$, and R_6 is branched C_6-C_{10} -alkylene, phenylene or phenylene substituted by from 1 to 3 methyl groups, benzylene or benzylene substituted by from 1 to 3 methyl groups, cyclohexylene or cyclohexylene substituted by from 1 to 3 methyl groups, cyclohexyl- CH_2 - or cyclohexyl- CH_2 - substituted by from 1 to 3 methyl groups.

30 [0024] Some examples of especially preferred functional photoinitiators are the compounds of formulae



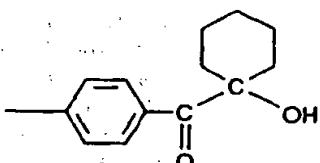
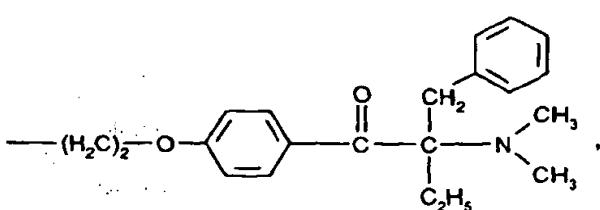
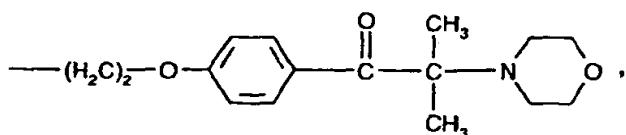
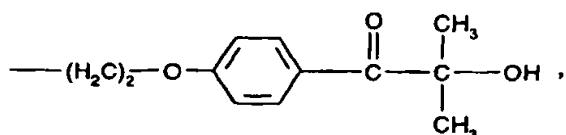


(11b),

or



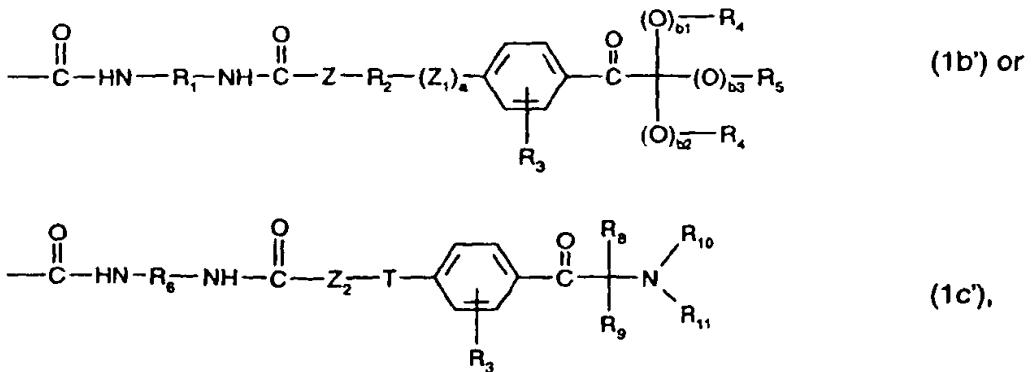
(11c),

wherein R₂₂ is a radical

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[0025] In a preferred embodiment of the invention, the covalent binding between the inorganic or preferably material surface and the photoinitiator occurs via reaction of a hydroxy, amino, alkylamino, thiol or carboxy group, particularly of a hydroxy or amino group, of the substrate surface with an isocyanato group of the photoinitiator, for example using a photoinitiator of the above formula (1b), (1c), (11a), (11b) or (11c). Suitable methods for this are known, for example, from the above-mentioned documents. The reaction may be carried out, for example, at elevated temperature, for example from 0° to 100°C and preferably at room temperature, and optionally in the presence of a catalyst. After the reaction, excess compounds can be removed, for example, with solvents.

[0026] According to a preferred embodiment of the invention the material to be coated is an organic polymer containing H-active groups, in particular -OH, -NH₂ and/or -NH-, on the surface that are coreactive with isocyanato groups, in some or all of them an H-atom having been substituted by a radical of formula



wherein for the variables R₁-R₁₁, T, Z, Z₁, Z₂, a, b1, b2 and b3 the above-given meanings and preferences apply.

20 [0027] According to another preferred embodiment of the invention, the covalent binding between the inorganic or preferably organic substrate and the photoinitiator occurs via reaction of a epoxy, carboxanhydride, lactone, azlactone or preferably isocyanato group of the substrate surface with a hydroxy, amino, alkylamino, thiol or carboxy group, particularly with a carboxy, hydroxy or amino group, of the photoinitiator, for example using a photoinitiator of the above formula (1a). This may be carried out, for example, by first reacting an above-mentioned bulk material containing H-active groups on the surface, in particular -OH, -NH₂ and/or -NH, selectively with one isocyanato group of a diisocyanate of 25 formula OCN-R₁-NCO, wherein R₁ has the above-given meanings, and then reacting the modified bulk material with a photoinitiator of the above-mentioned formula (1a).

30 [0028] Suitable reactive groups of the vinyl monomer according to step (a2) are, for example, a hydroxy, amino, carboxy, carboxylic acid ester, carboxylic acid anhydride, epoxy, lactone, azlactone or isocyanato group. One group of preferred reactive groups comprises carboxy, carboxylic acid anhydride, azlactone or isocyanato, in particular isocyanato. Another group of preferred reactive groups comprises amino or in particular hydroxy.

35 [0029] The vinyl monomer that is grafted onto the initiator-modified surface according to step (a2) is, for example, an ethylenically unsaturated compound having from 2 to 18 C-atoms and preferably from 2 to 10 C-atoms, which is substituted by a reactive group, wherein the above-given meanings and preferences apply.

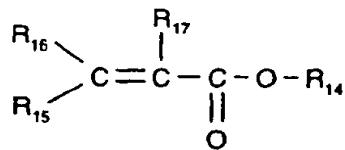
[0030] Suitable vinyl monomers having a reactive group are, for example, a compound of formula

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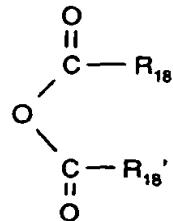
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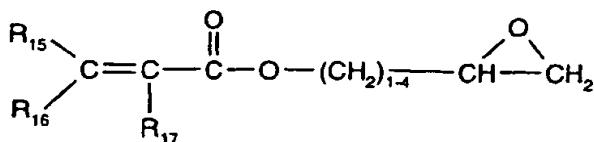
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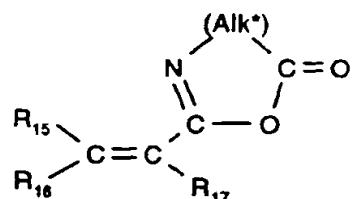
(2a),



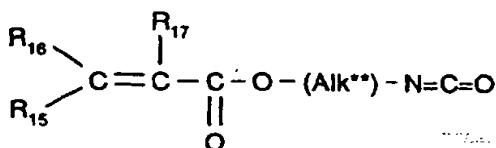
(2b),



(2c),



(2d) or



(2e),

40 wherein R_{14} is hydrogen, unsubstituted or hydroxy-substituted $\text{C}_1\text{-C}_6$ -alkyl or phenyl,
 R_{15} , and R_{16} are each independently of the other hydrogen, $\text{C}_1\text{-C}_4$ -alkyl, phenyl, carboxy or halogen,
 R_{17} is hydrogen, $\text{C}_1\text{-C}_4$ -alkyl or halogen,
 R_{18} and R_{18}' are each an ethylenically unsaturated radical having from 2 to 6 C-atoms, or
 R_{18} and R_{18}' together form a bivalent radical $-\text{C}(\text{R}_{15})=\text{C}(\text{R}_{17})-$ wherein R_{15} and R_{17} are as defined above, and
45 (Alk^*) is $\text{C}_1\text{-C}_6$ -alkylene, and (Alk^{**}) is $\text{C}_2\text{-C}_{12}$ -alkylene.

[0031] The following preferences apply to the variables contained in formulae (2a) - (2e):

50 R_{14} is preferably hydrogen or hydroxy- $\text{C}_1\text{-C}_4$ -alkyl, in particular hydrogen or β -hydroxyethyl.
One of the variables R_{15} and R_{16} is preferably hydrogen and the other one is hydrogen, methyl or carboxy. Most preferably R_{15} and R_{16} are each hydrogen.
 R_{17} is preferably hydrogen or methyl.
 R_{18} and R_{18}' are preferably each vinyl or 1-methylvinyl, or R_{18} and R_{18}' together form a radical $-\text{C}(\text{R}_{15})=\text{C}(\text{R}_{17})-$ wherein R_{15} and R_{17} are each independently hydrogen or methyl.
55 (Alk^*) is preferably methylene, ethylene or 1,1-dimethyl-methylene, in particular a radical $-\text{CH}_2-$ or $-\text{C}(\text{CH}_3)_2-$.
(Alk^{**}) is preferably $\text{C}_2\text{-C}_4$ -alkylene and in particular 1,2-ethylene.

[0032] Particularly preferred vinyl monomers having a reactive group are 2-isocyanatoethylmethacrylate (IEM), 2-

vinyl-azlactone, 2-vinyl-4,4-dimethyl-azlactone, acrylic acid, methacrylic acid, acrylic anhydride, maleic acid anhydride, 2-hydroxyethylacrylate (HEA), 2-hydroxymethacrylate (HEMA), glycidylacrylate or glycidylmethacrylate.

[0033] Throughout the application terms such as carboxy, carboxylic acid, -COOH, sulfo, -SO₃H, amino, -NH₂ and the like always include the free acid or amine as well as a suitable salt thereof, for example a biomedically or in particular occularly acceptable salt thereof such as, for example, a sodium, potassium, ammonium salt or the like (of an acid), or a hydrohalide such a hydrochloride (of an amine).

[0034] The vinyl monomer having a reactive group may be grafted as such or in admixture with a suitable vinyl comonomer, preferably a hydrophilic vinyl comonomer, onto the material surface.

[0035] The expression "hydrophilic vinyl comonomer" is understood to mean a monomer that typically produces as homopolymer a polymer that is water-soluble or capable of absorbing at least 10 % by weight water.

[0036] The proportion of vinyl comonomers, if used, is preferably from 0.1 to 3 units per vinyl monomer having a reactive group, especially from 0.25 to 3 units of vinyl comonomer per vinyl monomer having a reactive group and most preferably from 0.5 to 2 units per vinyl monomer having a reactive group.

[0037] Suitable hydrophilic vinyl comonomers include, without the following being an exhaustive list, C₁-C₂-alkyl acrylates and methacrylates, acrylamide, methacrylamide, N-mono- or N,N-di-C₁-C₂-alkylacrylamide and -methacrylamide, ethoxylated acrylates and methacrylates, sodium ethylenesulfonate, sodium styrenesulfonate, 2-acrylamido-2-methylpropanesulfonic acid, N-vinylpyrrole, N-vinylsuccinimide, five- to seven-membered N-vinyl lactams, 2- or 4-vinylpyridine, amino- (the term "amino" also including quaternary ammonium), mono-C₁-C₂-alkylamino- or di-C₁-C₂-alkylamino-C₁-C₂-alkyl acrylates and methacrylates, allyl alcohol and the like. Preferred are acrylamide, N,N-di-C₁-C₂-alkyl(meth)acrylamides such as N,N-dimethyl acrylamide or five- to seven-membered N-vinyl lactams such as N-vinylpyrrolidone.

[0038] In one embodiment of the invention the vinyl monomer having a reactive group is grafted to the initiator-modified material surface in the absence of a vinyl comonomer.

[0039] The vinyl monomer having a reactive group, optionally in admixture with a vinyl comonomer, may be applied to the initiator-modified material surface and polymerized there according to processes known per se. For example, the material is immersed in a solution of the vinyl monomer(s), or a layer of vinyl monomer(s) is first of all deposited on the modified material surface, for example, by dipping, spraying, spreading, knife coating, pouring, rolling, spin coating or vacuum vapor deposition. Suitable solvents, if used in the polymerization process, are, for example, water, C₁-C₄-alcohols such as methanol or ethanol, glycols such as ethylene glycol or dipolar aprotic solvents such as, for example, acetonitrile, N,N-dimethyl formamide (DMF), N-methyl pyrrolidone (NMP), dimethyl sulfoxide (DMSO), N,N-dimethyl acetamide or acetone. The polymerization of the vinyl monomer(s) on the material surface then may be initiated, for example, thermally by the action of heat or preferably by irradiation, particularly by UV radiation. Suitable light sources for the irradiation are known to the artisan and comprise for example mercury lamps, high pressure mercury lamps, xenon lamps, carbon arc lamps or sunlight. The time period of irradiation may depend, for example, on the desired properties of the resulting composite material but is usually in the range of up to 30 minutes, preferably from 10 seconds to 10 minutes, and particularly preferably from 0.5 to 5 minutes. It is advantageous to carry out the irradiation in an atmosphere of inert gas. After the polymerization, any non-covalently bound monomers, oligomers or polymers formed can be removed, for example by treatment with suitable solvents.

[0040] In case of a thermally initiated polymerization of the vinyl monomer(s) on the material surface said polymerization may be carried out, for example, at elevated temperature, for example at a temperature of from 35 to 100°C and preferably 40 to 80°C, for a time period of, for example, from 10 minutes to 48 hours and preferably 30 minutes to 36 hours in the absence or presence of one of the above-mentioned solvents. It is advantageous to carry out the thermally initiated polymerization in an atmosphere of inert gas.

[0041] By means of the polymerization step (a2), the vinyl monomer(s) may be grafted to the bulk material surface with formation of a primary coating comprising a plurality of polymer chains bound to the surface which form a so-called brush-type structure. Each polymer chain of said brush-type structure contains reactive groups at regular intervals (if the vinyl monomer comprising the reactive group is used without a vinyl comonomer) or statistically distributed (if the vinyl monomer comprising the reactive group is used in combination with a vinyl comonomer). The reactive groups that are present in the polymer chains are those mentioned before in the description of the vinyl monomers comprising a reactive group.

[0042] The reactive polymerization initiator of step (a3) is, for example, one of the thermal initiators or photoinitiators as mentioned in step (a1) wherein the above-given meanings and preferences apply. Preferred polymerization initiators of step (a3) are, in case of thermal initiators, azo-bis(C₂-C₁₂-alkanols) which are substituted by cyano, or are, in case of photoinitiators, compounds of the above formula (1a) wherein the above given meanings and preferences apply.

[0043] The reactions of the reactive groups of the polymer brushes obtained according to step (a2) with the polymerization initiator having co-reactive groups in step (a3) are well-known in the art and may be carried out as described in textbooks of organic chemistry. For example, in case that the primary coating is derived from a vinyl monomer of formula (2e) or the like, the reaction of its isocyanato groups with a compound of formula (1a) may be carried out in an

inert organic solvent such as acetonitrile, an optionally halogenated hydrocarbon, for example petroleum ether, methylcyclohexane, toluene, chloroform, methylene chloride and the like, or an ether, for example diethyl ether, tetrahydrofuran, dioxane, or a more polar solvent such as DMSO, DMA, N-methylpyrrolidone or even a lower alcohol or water, at a temperature of from 0 to 100°C, preferably from 0 to 50°C and particularly preferably at room temperature, optionally in the presence of a catalyst, for example a tertiary amine such as triethylamine or tri-n-butylamine, 1,4-diazabicyclooctane, or a tin compound such as dibutyltin dilaurate or tin dioctanoate. In addition, the reaction of the isocyanato groups of the polymer brushes with a compound of formula (1a) wherein HZ- is an amino group and a1 is 0, also may be carried out in an aqueous solution in the absence of a catalyst. It is advantageous to carry out the above reactions under an inert atmosphere, for example under a nitrogen or argon atmosphere.

5 [0044] In case that the polymer brushes are derived from a vinyl monomer of formula (2d) or the like, the reaction of the azlactone groups with a compound of formula (1a) wherein HZ- is an amino or hydroxy group and a1 is 0, may be carried out at room temperature or at elevated temperature, for example at about 20 to 75°C, in water, in a suitable organic solvent or mixtures thereof, for example in an aqueous medium or in an aprotic polar solvent such as DMF, DMSO, dioxane, acetonitrile and the like.

10 [0045] In case that the polymer brushes are derived from a vinyl monomer of formula (2c) or the like, the reaction of the epoxy groups with a compound of formula (1a) wherein HZ- is an amino group and a1 is 0, may be carried out, for example, at room temperature or at elevated temperature, for example at about 20 to 100°C, in water, in a suitable organic solvent or in mixtures thereof.

15 [0046] In case that the polymer brushes are derived from a vinyl monomer of formula (2c) or the like, the reaction of the epoxy groups with a compound of formula (1a) wherein HZ- is an hydroxy group and a1 is 0, may be carried out, for example, at room temperature or at elevated temperature, for example at about 20 to 100°C, in an aprotic medium using a base catalyst, for example $\text{Al}(\text{O-C}_1\text{-C}_6\text{-alkyl})_3$ or $\text{Ti}(\text{O-C}_1\text{-C}_6\text{-alkyl})_3$.

20 [0047] In case that the polymer brushes are derived from a vinyl monomer of formula (2b) or the like, the reaction of the carboxy anhydride with a compound of formula (1a) wherein X is an amino or hydroxy group and a1 is 0, may be carried out as described in organic textbooks, for example in an aprotic solvent, for example one of the above-mentioned aprotic solvents, at a temperature from room temperature to about 100°C.

25 [0048] In case that the polymer brushes are derived from a vinyl monomer of formula (2a) or the like, the reaction of its carboxy or hydroxy groups with a compound of formula (1a), wherein HZ-[C(O)]_{a1} - is amino, hydroxy or carboxy, may be carried out under the conditions that are customary for ester or amide formation,

30 [0049] In case that the primary coating is derived from a vinyl monomer of formula (2a) or the like, the reaction of its carboxy groups with a compound of formula (1a), wherein HZ-[C(O)]_{a1} - is amino or hydroxy, or the reaction of its amino or hydroxy groups with a compound of formula (1a), wherein HZ-[C(O)]_{a1} - is carboxy, may be carried out under the conditions that are customary for ester or amide formation, for example in an aprotic medium at a temperature from about room temperature to about 100°C. In case of a carboxy containing compound of formula (2a) it is preferred to carry out the esterification or amidation reaction in the presence of an activating agent, for example N-ethyl-N'-(3-dimethylaminopropyl)-carbodiimide (EDC), N-hydroxy succinimide (NHS) or N,N'-dicyclohexyl carbodiimide (DCC).

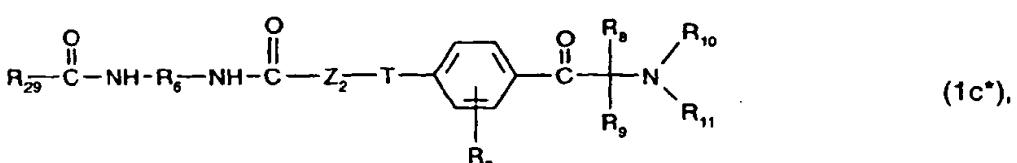
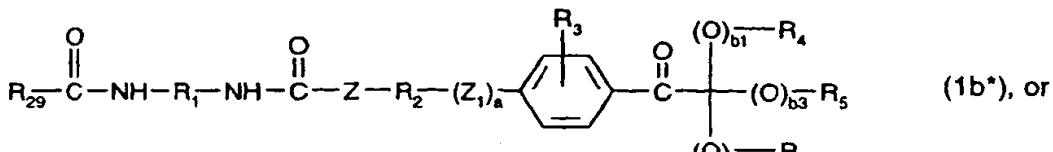
35 [0050] According to a further embodiment of the invention, the polymer brushes according to step

40 (a) of the process may be provided by

40 (a1) covalently binding polymerization initiator radicals to the surface; and
 (a2') graft polymerizing an ethylenically unsaturated polymerization initiator onto the initiator-modified material surface, wherein said ethylenically unsaturated polymerization initiator is a photoinitiator in case of a thermal initiator in step (a1), or is a thermal initiator in case of a photoinitiator in step (a1).

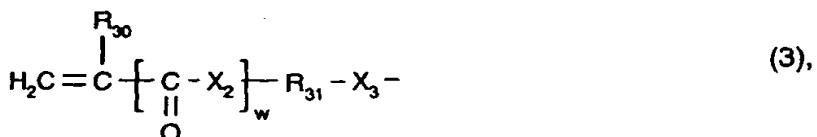
45 [0051] According to this embodiment of the invention, the polymerization initiator of step (a1) is preferably a thermal polymerization initiator, in particular one of the thermal polymerization initiators mentioned before; and the ethylenically unsaturated polymerization initiator of step (a2') is a photoinitiator.

[0052] A group of suitable photoinitiators according to step (a2') conforms, for example, to formula



15

20 wherein for R_1 , R_2 , R_3 , R_4 , R_5 , R_6 , R_8 , R_9 , R_{10} , R_{11} , T , Z , Z_1 , Z_2 , b_1 , b_2 and b_3 each the above given meanings and preferences apply, and R_{29} is a radical of formula



30

35 wherein R_{30} is hydrogen or methyl, R_{31} is C_1 - C_{12} -alkylene, C_1 - C_6 -alkylenephylene or phenylene- C_1 - C_6 -alkylene, or if w is 0 may also be a direct bond, w is 0 or 1, and X_2 and X_3 are each independently of the other -O- or -NH-. R_{31} is preferably linear or branched C_2 - C_6 -alkylene, more preferably linear C_2 - C_4 -alkylene, and in particular 1,2-ethylene. w is preferably an integer of 1.

[0053] ... The compounds of formulae (1b*) and (1c*) are known, for example, from PCT application WO96/20919 or from U.S. patent No. 5,527,925.

[0054] The ethylenically unsaturated polymerization initiator may be applied to the initiator-modified material surface and polymerized there, for example, in analogy to the graft polymerization of the vinyl monomer having a reactive group as described above.

[0055] By means of the above described reaction step (a) of the process of the invention, the material surface is provided with a plurality of polymer brushes comprising polymerization initiator radicals. Each polymer chain of said brush-type structure contains polymerization initiator radicals at regular intervals (if the vinyl monomer comprising the reactive group is used without a vinyl comonomer, or if an ethylenically unsaturated polymerization initiator is used) or 45 statistically distributed (if the vinyl monomer comprising the reactive group is used in combination with a vinyl comonomer).

[0056] A hydrophilic monomer in step (b) of the invention is understood to mean a monomer that typically produces as homopolymer a polymer that is water-soluble or capable of absorbing at least 10 % by weight water.

50 **[0057]** Suitable hydrophilic vinyl comonomers include, without the following being an exhaustive list, hydroxy-substituted C₁-C₄-alkyl acrylates and methacrylates, acrylamide, methacrylamide, mono- or di-C₁-C₄ alkylacrylamides and -methacrylamides, ethoxylated acrylates and methacrylates, hydroxy-substituted C₁-C₄-alkylacrylamides and methacrylamides, hydroxy-substituted C₁-C₄-alkyl vinyl ethers, sodium ethylenesulfonate, sodium styrenesulfonate, 2-acrylamido-2-methylpropanesulfonic acid, N-vinylpyrrole, N-vinylsuccinimide, N-vinylpyrrolidone, 2- or 4-vinylpyridine, 55 vinylically unsaturated carboxylic acids having a total of from 3 to 5 carbon atoms, amino- (the term "amino" also including quaternary ammonium), mono-C₁-C₄-alkylamino- or di-C₁-C₄-alkylamino-C₁-C₄-alkyl acrylates and methacrylates, vinylacetate, allyl alcohol and the like. Preferred are, for example, hydroxy-substituted C₂-C₄alkyl (meth)acrylates, five- to seven-membered N-vinyl lactams, N,N-di-C₁-C₄-alkyl(meth)acrylamides, acrylic acid and methacrylic acid.

[0058] Examples of suitable hydrophilic vinyl comonomers include hydroxyethyl methacrylate, hydroxyethyl acrylate, acrylamide, methacrylamide, N,N-dimethylacrylamide, allyl alcohol, vinylpyridine, N-vinylpyrrolidone, glycerol methacrylate, N-(1,1-dimethyl-3-oxobutyl)-acrylamide and the like. Preferred hydrophilic vinyl comonomers are 2-hydroxyethyl methacrylate, N-vinylpyrrolidone, N,N-dimethylacrylamide and acrylamide.

5 [0059] A suitable macromonomer according to step (b) of the process of the invention is, for example, of formula



15 R_{32} is hydrogen, C_1 - C_6 -alkyl or a radical $-COOR'$;
 R, R' and R_{32} are each independently of the other hydrogen or C_1 - C_6 -alkyl;
 A is a direct bond or is a radical of formula



or



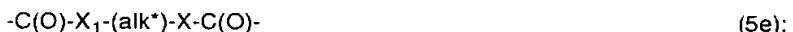
or



or

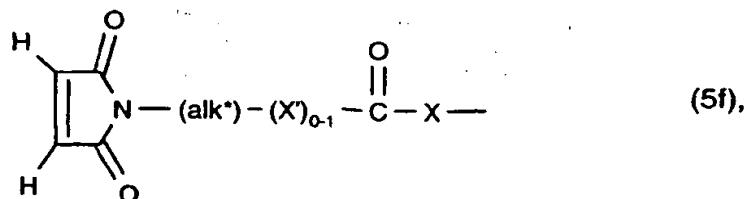


or



or

45 A and R_{32} , together with the adjacent double bond, are a radical of formula



50 A_1 is $-O-C_2-C_{12}$ -alkylene which is unsubstituted or substituted by hydroxy, or is $-O-C_2-C_{12}$ -alkylene- $NH-C(O)-$ or $-O-C_2-C_{12}$ -alkylene- $O-C(O)-NH-R_{33}-NH-C(O)-$ or $-NH-(Alk^*)-C(O)-$, wherein (Alk*) is as defined above and R_{33} is linear or branched C_1 - C_{18} -alkylene or unsubstituted or C_1 - C_4 -alkyl- or C_1 - C_4 -alkoxy-substituted C_6 - C_{10} -arylene, C_7 - C_{18} -aralkylene, C_6 - C_{10} -arylene- C_1 - C_2 -alkylene- C_6 - C_{10} -arylene, C_3 - C_8 -cycloalkylene, C_3 - C_8 -cycloalkylene- C_1 -alkylene, C_3 - C_8 -cycloalkylene- C_1 - C_2 -alkylene- C_3 - C_8 -cycloalkylene or C_1 - C_6 -alkylene- C_3 - C_8 -cycloalkylene- C_1 - C_6 -alkylene;

55 A_2 is C_1 - C_8 -alkylene; phenylene or benzylene;

m and n are each independently of the other the number 0 or 1;

X, X_1 and X' are each independently of the other a bivalent group $-O-$ or $-NR''$, wherein R'' is hydrogen or C_1 - C_6 -

alkyl;

(alk*) is C₂-C₁₂-alkylene;
and (oligomer) denotes

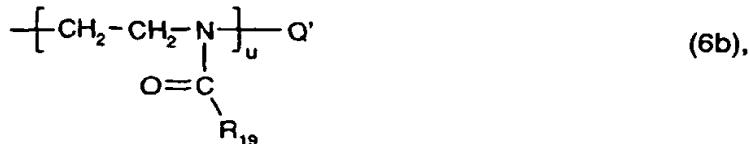
5 (i) the radical of a telomer of formula



10

wherein (alk) is C₂-C₁₂-alkylene,
Q is a monovalent group that is suitable to act as a polymerization chain-reaction terminator,
15 p and q are each independently of another an integer from 0 to 350, wherein the total of (p+q) is an integer from 2 to 350,
and B and B' are each independently of the other a 1,2-ethylene radical derivable from a copolymerizable vinyl monomer by replacing the vinylic double bond by a single bond, at least one of the radicals B and B'
20 being substituted by a hydrophilic substituent; or

20 (ii) the radical of an



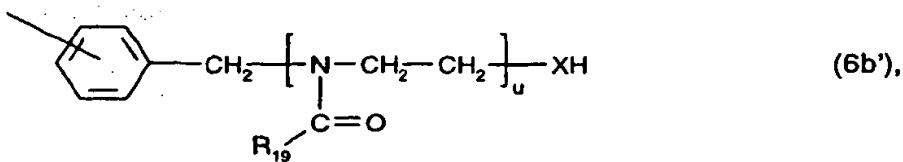
25

30 oligomer of the formula

wherein R₁₉ is hydrogen or unsubstituted or hydroxy-substituted C₁-C₁₂-alkyl, u is an integer from 2 to 250 and Q' is a radical of a polymerization initiator; or

35

(iii) the radical of formula

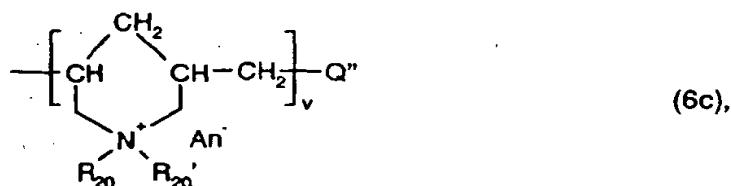


40

45 wherein R₁₉, X and u are as defined above, or

50

(iv) the radical of an oligomer of formula



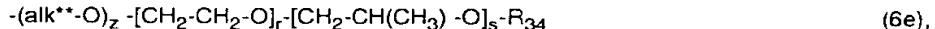
5 wherein R_{20} and R_{20}' are each independently C_1 - C_4 -alkyl, An^- is an anion, v is an integer from 2 to 250, and Q'' is a monovalent group that is suitable to act as a polymerization chain-reaction terminator; or

10 (v) the radical of an oligopeptide of formula



25 wherein R_{21} is hydrogen or C_1 - C_4 -alkyl which is unsubstituted or substituted by hydroxy, carboxy, carbamoyl, amino, phenyl, o-, m- or p-hydroxyphenyl, imidazolyl, indolyl or a radical $-NH-C(=NH)-NH_2$ and t is an integer from 2 to 250, or the radical of an oligopeptide based on proline or hydroxyproline; or

30 (vi) the radical of a polyalkylene oxide of formula



40 wherein R_{34} is hydrogen or C_1 - C_{24} -alkyl, (alk^{**}) is C_2 - C_4 -alkylene, z is 0 or 1, r and s are each independently an integer from 0 to 250 and the total of $(r+s)$ is from 2 to 250; or

45 (vii) the radical of an oligosaccharide;
subject to the provisos that

50 A is not a direct bond if (oligomer) is a radical of formula (6a);

55 A is a radical of formula (5a), (5b) or (5d) or A and R_{32} , together with the adjacent double bond, are a radical of formula (5f) if (oligomer) is a radical of formula (6b), (6c), (6d) or (6e) or is the radical of an oligosaccharide;

60 A is a direct bond if (oligomer) is a radical of formula (6b'); and

65 A is a radical of formula (5c) or (5e) if (oligomer) is a radical of formula (6d').

70 [0060] The following preferences apply to the variables contained in the definition of the macromonomer of formula (4):

75 R' is preferably hydrogen or C_1 - C_4 -alkyl, more preferably hydrogen or C_1 - C_2 -alkyl and particularly preferably hydrogen.

80 R_{32} is preferably hydrogen, methyl or carboxyl, and particularly preferably hydrogen.

85 R is preferably hydrogen or methyl.

90 X is preferably a bivalent group $-O-$ or $-NH-$. X is particularly preferably the group $-NH-$ if (oligomer) is a radical of formula (6a); (6c) or (6d), and is particularly preferably the group $-O-$ if (oligomer) is a radical of formula (6b) or (6e) or is the radical of an oligosaccharide. X' is preferably $-O-$ or $-NH-$ and more preferably $-NH-$. X_1 is preferably $-O-$ or $-NH-$.

95 R_{33} as alkylene is preferably a linear or branched C_3 - C_{14} alkylene radical, more preferably a linear or branched C_4 - C_{12} alkylene radical and most preferably a linear or branched C_6 - C_{10} -alkylene radical. Some preferred alkylene radicals are 1,4-butylene, 2,2-dimethyl-1,4-butylene, 1,5-pentylene, 2,2-dimethyl-1,5-pentylene, 1,6-hexylene, 2,2,3- or 2,2,4-trimethyl-1,5-pentylene, 2,2-dimethyl-1,6-hexylene, 2,2,3- or 2,2,4- or 2,2,5-trimethyl-1,6-hexylene, 2,2-dimethyl-1,7-heptylene, 2,2,3- or 2,2,4- or 2,2,5- or 2,2,6-trimethyl-1,7-heptylene, 1,8-octylene, 2,2-dimethyl-1,8-octylene and 2,2,3- or 2,2,4- or 2,2,5- or 2,2,6- or 2,2,7-trimethyl-1,8-octylene.

100 [0061] When R_{33} is arylene, it is, for example, naphthylene or especially phenylene, each of which may be substituted, for example, by C_1 - C_4 -alkyl or by C_1 - C_4 -alkoxy. Preferably, R_{33} as arylene is 1,3- or 1,4-phenylene that is unsubstituted or substituted by C_1 - C_4 -alkyl or by C_1 - C_4 -alkoxy in the ortho-position to at least one linkage site.

105 [0062] R_{33} as aralkylene is preferably naphthylalkylene and most preferably phenylalkylene. The alkylene group in aralkylene contains preferably from 1 to 12, more preferably from 1 to 6 and most preferably from 1 to 4 carbon atoms.

Most preferably, the alkylene group in aralkylene is methylene or ethylene.

[0063] When R_{33} is cycloalkylene, it is preferably C_5 - C_6 -cycloalkylene and most preferably cyclohexylene that is unsubstituted or substituted by methyl.

[0064] When R_{33} is cycloalkylene-alkylene, it is preferably cyclopentylene- C_1 - C_4 -alkylene and especially cyclohexylene- C_1 - C_4 -alkylene, each unsubstituted or mono- or poly-substituted by C_1 - C_4 -alkyl, especially methyl. More preferably, the group cycloalkylene-alkylene is cyclohexylene-ethylene and, most preferably, cyclohexylene-methylene, each unsubstituted or substituted in the cyclohexylene radical by from 1 to 3 methyl groups.

[0065] When R_{33} is alkylene-cycloalkylene-alkylene, it is preferably C_1 - C_4 -alkylene-cyclopentylene- C_1 - C_4 -alkylene and especially C_1 - C_4 -alkylene-cyclohexylene- C_1 - C_4 -alkylene, each unsubstituted or mono- or poly-substituted by C_1 - C_4 -alkyl, especially methyl. More preferably, the group alkylene-cycloalkylene-alkylene is ethylene-cyclohexylene-ethylene and, most preferably, is methylene-cyclohexylene-methylene, each unsubstituted or substituted in the cyclohexylene radical by from 1 to 3 methyl groups.

[0066] R_{33} as C_3 - C_8 -cycloalkylene- C_1 - C_2 -alkylene- C_3 - C_8 -cycloalkylene or C_6 - C_{10} -arylene- C_1 - C_2 -alkylene- C_6 - C_{10} -arylene is preferably C_5 - C_6 -cycloalkylene-methylene- C_5 - C_6 -cycloalkylene or phenylene-methylene-phenylene, each of which may be unsubstituted or substituted in the cycloalkyl or phenyl ring by one or more methyl groups.

[0067] The radical R_{33} has a symmetrical or, preferably, an asymmetrical structure. A preferred group of radicals R_{11} comprises those, wherein R_{33} is linear or branched C_6 - C_{10} alkylene; cyclohexylene-methylene or cyclohexylene-methylene-cyclohexylene each unsubstituted or substituted in the cyclohexyl moiety by from 1 to 3 methyl groups; or phenylene or phenylene-methylene-phenylene each unsubstituted or substituted in the phenyl moiety by methyl. The bivalent radical R_{33} is derived preferably from a diisocyanate and most preferably from a diisocyanate selected from the group isophorone diisocyanate (IPDI), toluylene-2,4-diisocyanate (TDI), 4,4'-methylenebis(cyclohexyl isocyanate), 1,6-diisocyanato-2,2,4-trimethyl-n-hexane (TMDI), methylenebis(phenyl isocyanate), methylenebis(cyclohexyl-4-isocyanate) and hexamethylene diisocyanate (HMDI).

[0068] Preferred meanings of A_1 are unsubstituted or hydroxy-substituted - O - C_2 - C_8 -alkylene or a radical - O - C_2 - C_6 -alkylene- NH - $C(O)$ - and particularly - O -(CH_2)₂₋₄-, - O - CH_2 - $CH(OH)$ - CH_2 - or a radical - O -(CH_2)₂₋₄- NH - $C(O)$ -.

[0069] A_2 is preferably C_1 - C_6 -alkylene, phenylene or benzylene, more preferably C_1 - C_4 -alkylene and even more preferably C_1 - C_2 -alkylene.

n is an integer of 0 or preferably 1. m is preferably an integer of 1.

[0070] R_{32}' is preferably hydrogen or methyl and particularly preferably hydrogen.

In case that (oligomer) is a radical of formula (6a), (6b), (6c), (6d) or (6e) or is the radical of an oligosaccharide, is A preferably a radical of formula (5a) or (5b) and particularly preferably a radical of formula (5a), wherein the above given meanings and preferences apply for the variables contained therein.

A preferred group of hydrophilic macromonomers according to the invention comprises compounds of the above formula (4), wherein R is hydrogen or methyl, R_{32} is hydrogen, methyl or carboxyl, R_{32}' is hydrogen, A is a radical of the formula (5a) or (5b) and (oligomer) is a radical of formula (6a), (6b), (6c), (6d) or (6e) or is the radical of an oligosaccharide. An even more preferred group of hydrophilic macromonomers comprises compounds of the above formula (4), wherein R is hydrogen or methyl, R_{32} and R_{32}' are each hydrogen, A is a radical of the formula (5a) and (oligomer) is a radical of formula (6a). A further group of preferred macromonomers comprises compounds of formula (4), wherein A is a radical of formula (5e) above and (oligomer) is a radical of formula (6a).

[0070] (alk) and (alk*) are each independently preferably C_2 - C_8 -alkylene, more preferably C_2 - C_6 -alkylene, even more preferably C_2 - C_4 -alkylene and particularly preferably 1,2-ethylene. The alkylene radicals (alk) and (alk*) may be branched or preferably linear alkylene radicals.

[0071] Q is for example hydrogen.

[0072] The total of (p+q) is preferably an integer from 2 to 150, more preferably from 5 to 100, even more preferably from 5 to 75 and particularly preferably from 10 to 50. In a preferred embodiment of the invention q is 0 and p is an integer from 2 to 250, preferably from 2 to 150, more preferably from 5 to 100, even more preferably from 5 to 75 and particularly preferably from 10 to 50.

[0073] Suitable hydrophilic substituents of the radicals B or B' may be non-ionic, anionic, cationic or zwitterionic substituents. Accordingly, the telomer chain of formula (5a) that contains monomer units B and/or B' may be a charged chain containing anionic, cationic and/or zwitterionic groups or may be an uncharged chain. In addition, the telomer chain may comprise a copolymeric mixture of uncharged and charged units. The distribution of the charges within the telomer, if present, may be random or blockwise.

[0074] In one preferred embodiment of the invention, the telomer radical of formula (6a) is composed solely of non-ionic monomer units B and/or B'. In another preferred embodiment of the invention, the telomer radical of formula (6a) is composed solely of ionic monomer units B and/or B', for example solely of cationic monomer units or solely of anionic monomer units. Still another preferred embodiment of the invention is directed to telomer radicals of formula (6a) comprising nonionic units B and ionic units B'.

[0075] Suitable non-ionic substituents of B or B' include for example a radical C₁-C₆-alkyl which is substituted by one or more same or different substituents selected from the group consisting of -OH, C₁-C₄-alkoxy and -NR₂₃R_{23'}, wherein R₂₃ and R_{23'} are each independently of another hydrogen or unsubstituted or hydroxy-substituted C₁-C₆-alkyl or phenyl; phenyl which is substituted by hydroxy, C₁-C₄-alkoxy or -NR₂₃R_{23'}, wherein R₂₃ and R_{23'} are as defined above; a radical -COOY, wherein Y is C₁-C₂₄-alkyl which is unsubstituted or substituted, for example, by hydroxy, C₁-C₄-alkoxy, -O-Si(CH₃)₃, -NR₂₃R_{23'} wherein R₂₃ and R_{23'} are as defined above, a radical -O-(CH₂CH₂O)₁₋₂₄-E wherein E is hydrogen or C₁-C₆-alkyl, or a radical -NH-C(O)-O-G, wherein -O-G is the radical of a saccharide with 1 to 8 sugar units or is a radical -O-(CH₂CH₂O)₁₋₂₄-E, wherein E is as defined above, or Y is C₅-C₈-cycloalkyl which is unsubstituted or substituted by C₁-C₄-alkyl or C₁-C₄-alkoxy, or is unsubstituted or C₁-C₄-alkyl- or C₁-C₄-alkoxy-substituted phenyl or C₇-C₁₂-aralkyl; -CONY₁Y₂ wherein Y₁ and Y₂ are each independently hydrogen, C₁-C₁₂-alkyl, which is unsubstituted or substituted for example by hydroxy, C₁-C₄-alkoxy or a radical -O-(CH₂CH₂O)₁₋₂₄-E wherein E is as defined above, or Y₁ and Y₂ together with the adjacent N-atom form a five- or six-membered heterocyclic ring having no additional heteroatom or one additional oxygen or nitrogen atom; a radical -OY₃, wherein Y₃ is hydrogen; or C₁-C₁₂-alkyl which is unsubstituted or substituted by -NR₂₃R_{23'}; or is a radical -C(O)-C₁-C₄-alkyl; and wherein R₂₃ and R_{23'} are as defined above; or a five- to seven-membered heterocyclic radical having at least one N-atom and being bound in each case via said nitrogen atom.

[0076] Suitable anionic substituents of B or B' include for example C₁-C₆-alkyl which is substituted by -SO₃H, -OSO₃H, -OPO₃H₂ and -COOH; phenyl which is substituted by one or more same or different substituents selected from the group consisting of -SO₃H, -COOH, -OH and -CH₂-SO₃H; -COOH; a radical -COOY₄, wherein Y₄ is C₁-C₂₄-alkyl which is substituted for example by -COOH, -SO₃H, -OSO₃H, -OPO₃H₂ or by a radical -NH-C(O)-O-G' wherein G' is the radical of an anionic carbohydrate; a radical -CONY₅Y₆ wherein Y₅ is C₁-C₂₄-alkyl which is substituted by -COOH, -SO₃H, -OSO₃H, or -OPO₃H₂ and Y₆ independently has the meaning of Y₅ or is hydrogen or C₁-C₁₂-alkyl; or -SO₃H; or a salt thereof, for example a sodium, potassium, ammonium or the like salt thereof.

[0077] Suitable cationic substituents of B or B' include C₁-C₁₂-alkyl which is substituted by a radical -NR₂₃R_{23'}R_{23''}"An", wherein R₂₃, R_{23'} and R_{23''} are each independently of another hydrogen or unsubstituted or hydroxy-substituted C₁-C₆-alkyl or phenyl, and An" is an anion; or a radical -C(O)OY₇, wherein Y₇ is C₁-C₂₄-alkyl which is substituted by -NR₂₃R_{23'}R_{23''}"An" and is further unsubstituted or substituted for example by hydroxy, wherein R₂₃, R_{23'}, R_{23''} and An" are as defined above.

[0078] Suitable zwitterionic substituents of B or B' include a radical -R₂₄-Zw, wherein R₂₄ is a direct bond or a functional group, for example a carbonyl, carbonate, amide, ester, dicarboanhydride, dicarboimide, urea or urethane group; and Zw is an aliphatic moiety comprising one anionic and one cationic group each.

[0079] The following preferences apply to the hydrophilic substituents of B and B':

(i) non-ionic substituents:

[0080] Preferred alkyl substituents of B or B' are C₁-C₄-alkyl, in particular C₁-C₂-alkyl, which is substituted by one or more substituents selected from the group consisting of -OH and -NR₂₃R_{23'}, wherein R₂₃ and R_{23'} are each independently of another hydrogen or C₁-C₄-alkyl, preferably hydrogen, methyl or ethyl and particularly preferably hydrogen or methyl, for example -CH₂-NH₂, -CH₂-N(CH₃)₂.

Preferred phenyl substituents of B or B' are phenyl which is substituted by -NH₂ or N(C₁-C₂-alkyl)₂, for example o-, m- or p-aminophenyl.

In case that the hydrophilic substituent of B or B' is a radical -COOY, Y as optionally substituted alkyl is preferably C₁-C₁₂-alkyl, more preferably C₁-C₆-alkyl, even more preferably C₁-C₄-alkyl and particularly preferably C₁-C₂-alkyl, each of which being unsubstituted or substituted as mentioned above. In case that the alkyl radical Y is substituted by -NR₂₃R_{23'}, the above-given meanings and preferences apply for R₂₃ and R_{23'}. Examples of suitable saccharide substituents -O-G of the alkyl radical Y that is substituted by -NH-C(O)-O-G are the radical of a mono- or disaccharide, for example glucose, acetyl glucose, methyl glucose, glucosamine, N-acetyl glucosamine, glucono lactone, mannose, galactose, galactosamine, N-acetyl galactosamine, fructose, maltose, lactose, fucose, saccharose or trehalose, the radical of an anhydrosaccharide such as levoglucosan, the radical of a glucosid such as octylglucosid, the radical of a sugar alcohol such as sorbitol, the radical of a sugar acid derivative such as lactobionic acid amide, or the radical of an oligosaccharide with a maximum of 8 sugar units, for example fragments of a cyclodextrin, starch, chitosan, maltotriose or maltohexaose. The radical -O-G preferably denotes the radical of a mono- or disaccharide or the radical of a cyclodextrin fragment with a maximum of 8 sugar units. Particular preferred saccharide radicals -O-G are the radical of trehalose or the radical of a cyclodextrin fragment. In case that the alkyl radical Y is substituted by a radical -O-(CH₂CH₂O)₁₋₂₄-E or -NH-C(O)-O-G wherein -O-G is -O-(CH₂CH₂O)₁₋₂₄-E, the number of (CH₂CH₂O) units is preferably from 1 to 12 in each case and more preferably from 2 to 8. E is preferably hydrogen or C₁-C₂-alkyl.

Y as C₅-C₈-cycloalkyl is for example cyclopentyl or preferably cyclohexyl, each of which being unsubstituted or substituted for example by 1 to 3 C₁-C₂-alkyl groups. Y as C₇-C₁₂-aralkyl is for example benzyl.

[0081] Preferred nonionic radicals -COOY are those wherein Y is C₁-C₆-alkyl; or C₂-C₆-alkyl which is substituted by one or two substituents selected from the group consisting of hydroxy; ; C₁-C₂-alkoxy; -O-Si(CH₃)₃; and -NR₂₃R₂₃' wherein R₂₃ and R₂₃' are each independently of another hydrogen or C₁-C₄-alkyl; or Y is a radical -CH₂CH₂-O-(CH₂CH₂O)₁₋₁₂-E wherein E is hydrogen or C₁-C₂-alkyl; or is a radical -C₂-C₄-alkylene-NH-C(O)-O-G, wherein -O-G is the radical of a saccharide.

[0082] More preferred non-ionic radicals -COOY are those wherein Y is C₁-C₄-alkyl; or C₂-C₄-alkyl which is substituted by one or two substituents selected from the group consisting of -OH and -NR₂₃R₂₃' wherein R₂₃ and R₂₃' are each independently of another hydrogen or C₁-C₂-alkyl; or a radical -CH₂CH₂-O-(CH₂CH₂O)₁₋₁₂-E wherein E is hydrogen or C₁-C₂-alkyl; or is a radical -C₂-C₄-alkylene-NH-C(O)-O-G wherein -O-G is the radical of a saccharide.

[0083] Particularly preferred radicals -COOY comprise those wherein Y is C₁-C₂-alkyl, particularly methyl; or C₂-C₃-alkyl, which is unsubstituted or substituted by hydroxy or N,N-di-C₁-C₂-alkylamino, or is a radical -C₂-C₃-alkylene-NH-C(O)-O-G wherein -O-G is the radical of trehalose or the radical of a cyclodextrin fragment with a maximum of 8 sugar units.

[0084] Preferred non-ionic substituents -C(O)-NY₁Y₂ of B or B' are those wherein Y₁ and Y₂ are each independently of the other hydrogen or C₁-C₆-alkyl which is unsubstituted or substituted by hydroxy; or Y₁ and Y₂ together with the adjacent N-atom form a heterocyclic 6-membered ring having no further heteroatom or having one further N- or O-atom. Even more preferred meanings of Y₁ and Y₂, independently of each other, are hydrogen or C₁-C₄-alkyl which is unsubstituted or substituted by hydroxy; or Y₁ and Y₂ together with the adjacent N-atom form a N-C₁-C₂-alkylpiperazino or morpholino ring. Particularly preferred non-ionic radicals -C(O)-NY₁Y₂ are those wherein Y₁ and Y₂ are each independently of the other hydrogen or C₁-C₂-alkyl; or Y₁ and Y₂ together with the adjacent N-atom form a morpholino ring.

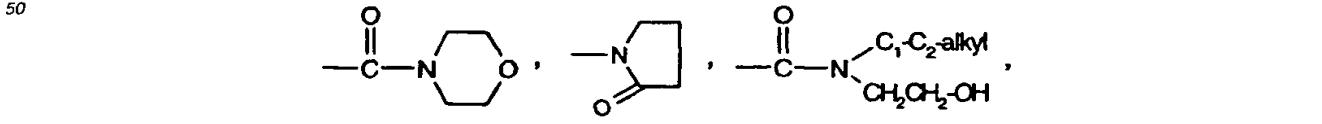
[0085] Preferred non-ionic substituents -OY₃ of B or B' are those wherein Y₃ is hydrogen, C₁-C₄-alkyl which is unsubstituted or substituted by -NH₂ or -N(C₁-C₂-alkyl)₂, or is a group -C(O)C₁-C₂-alkyl. Y₃ is particularly preferred hydrogen or acetyl.

[0086] Preferred non-ionic heterocyclic substituents of B or B' are a 5- or 6-membered heteroaromatic or heteroaliphatic radical having one N-atom and in addition no further heteroatom or an additional N- or O- heteroatom, or is a 5 to 7-membered lactame. Examples of such heterocyclic radicals are N-pyrrolidonyl, 2- or 4-pyridinyl, 2-methyl pyridin-5-yl, 2-, 3- oder 4-hydroxypyridinyl, N-ε-caprolactamyl, N-imidazolyl, 2-methylimidazol-1-yl, N-morpholiny or 4-N-methylpiperazin-1-yl, particularly N-morpholiny or N-pyrrolidonyl.

[0087] A group of preferred non-ionic substituents of B or B' comprises C₁-C₂-alkyl, which is unsubstituted or substituted by -OH or -NR₂₃R₂₃', wherein R₂₃ and R₂₃' are each independently of the other hydrogen or C₁-C₂-alkyl; a radical -COOY wherein Y is C₁-C₄-alkyl; C₂-C₄-alkyl which is substituted by -OH, -NR₂₃R₂₃' wherein R₂₃ and R₂₃' are each independently of another hydrogen or C₁-C₂-alkyl, or Y is a radical -C₂-C₄-alkylene-NH-C(O)-O-G wherein -O-G is the radical of a saccharide; a radical -C(O)-NY₁Y₂, wherein Y₁ and Y₂ are each independently of the other hydrogen or C₁-C₆-alkyl which is unsubstituted or substituted by hydroxy, or Y₁ and Y₂ together with the adjacent N-atom form a heterocyclic 6-membered ring having no further heteroatom or having one further N- or O-atom; a radical -OY₃, wherein Y₃ is hydrogen, C₁-C₄-alkyl which is unsubstituted or substituted by -NH₂ or -N(C₁-C₂-alkyl)₂, or is a group -C(O)C₁-C₂-alkyl; or a 5- or 6-membered heteroaromatic or heteroaliphatic radical having one N-atom and in addition no further heteroatom or an additional N-, O- or S-heteroatom, or a 5 to 7-membered lactame.

[0088] A group of more preferred non-ionic substituents of B or B' comprises a radical -COOY, wherein Y is C₁-C₂-alkyl, C₂-C₃-alkyl, which is substituted by hydroxy, amino or N,N-di-C₁-C₂-alkylamino, or is a radical -C₂-C₄-alkylene-NH-C(O)-O-G wherein -O-G is the radical of trehalose or a cyclodextrin fragment with a maximum of 8 sugar units; a radical -CO-NY₁Y₂, wherein Y₁ and Y₂ are each independently of the other hydrogen or C₁-C₄-alkyl which is unsubstituted or substituted by hydroxy, or Y₁ and Y₂ together with the adjacent N-atom form a N-C₁-C₂-alkylpiperazino or morpholino ring; or a heterocyclic radical selected from the group consisting of N-pyrrolidonyl, 2- or 4-pyridinyl, 2-methylpyridin-5-yl, 2-, 3- oder 4-hydroxypyridinyl, N-ε-caprolactamyl, N-imidazolyl, 2-methylimidazol-1-yl, N-morpholiny and 4-N-methylpiperazin-1-yl.

[0089] A particularly preferred group of non-ionic substituents of B or B' comprises the radicals -CONH₂, -CON(CH₃)₂,



55 -CONH-(CH₂)₂-OH, -COO-(CH₂)₂-N(CH₃)₂, and -COO(CH₂)₂₋₄-NHC(O)-O-G wherein -O-G is the radical of trehalose.

(ii) anionic substituents:

[0090] Preferred anionic substituents of B or B' are C₁-C₄-alkyl, in particular C₁-C₂-alkyl, which is substituted by one or more substituents selected from the group consisting of -SO₃H and -OPO₃H₂, for example -CH₂-SO₃H; phenyl which is substituted by -SO₃H or sulfomethyl, for example o-, m- or p-sulfophenyl or o-, m- or p-sulfomethylphenyl; -COOH; a radical -COOY₄, wherein Y₄ is C₂-C₆-alkyl which is substituted by -COOH, -SO₃H, -OSO₃H, -OPO₃H₂, or by a radical -NH-C(O)-O-G' wherein G' is the radical of lactobionic acid, hyaluronic acid or sialic acid, in particular C₂-C₄-alkyl which is substituted by -SO₃H or -OSO₃H; a radical -CONY₅Y₆ wherein Y₅ is C₁-C₆-alkyl substituted by sulfo, in particular C₂-C₄-alkyl substituted by sulfo, and Y₆ is hydrogen, for example the radical -C(O)-NH-C(CH₃)₂-CH₂-SO₃H; or -SO₃H; or a suitable salt thereof. Particular preferred anionic substituents of B or B' are -COOH, -SO₃H, o-, m- or p-sulfophenyl, o-, m- or p-sulfomethylphenyl or a radical -CONY₅Y₆ wherein Y₅ is C₂-C₄-alkyl substituted by sulfo, and Y₆ is hydrogen.

(iii) cationic substituents:

[0091] Preferred cationic substituents of B or B' are C₁-C₄-alkyl, in particular C₁-C₂-alkyl, which is in each case substituted by -NR₂₃R₂₃'R₂₃"⁺An⁻; or a radical -C(O)OY₇ wherein Y₇ is C₂-C₆-alkyl, in particular C₂-C₄-alkyl, which is in each case substituted by -NR₂₃R₂₃'R₂₃"⁺An⁻ and is further unsubstituted or substituted by hydroxy. R₂₃, R₂₃' and R₂₃" are each independently of another preferably hydrogen or C₁-C₄-alkyl, more preferably methyl or ethyl and particularly preferably methyl. Examples of suitable anions An⁻ are Hal⁻, wherein Hal is halogen, for example Br⁻, F⁻, J⁻ or particularly Cl⁻, furthermore HCO₃⁻, CO₃²⁻, H₂PO₄⁻, HPO₄²⁻, PO₄³⁻, HSO₄⁻, SO₄²⁻ or the radical of an organic acid such as OCOCH₃⁻ and the like. A particularly preferred cationic substituent of B or B' is a radical -C(O)OY₇ wherein Y₇ is C₂-C₄-alkyl, which is substituted by -N(C₁-C₂-alkyl)₃⁺An⁻ and is further substituted by hydroxy, and An⁻ is an anion, for example the radical -C(O)O-CH₂-CH(OH)-CH₂-N(CH₃)₃⁺An⁻.

(iv) zwitterionic substituents -R₂₄-Zw:

[0092] R₂₄ is a preferably a carbonyl, ester or amide functional group and more preferably an ester group -C(O)-O-. Suitable anionic groups of the moiety Zw are for example -COO⁻, -SO₃⁻, -OSO₃⁻, -OPO₃H⁻ or bivalent -O-PO₂²⁻ or -O-PO₂²⁻-O-, preferably a group -COO⁻ or -SO₃⁻ or a bivalent group -O-PO₂²⁻, and in particular a group -SO₃⁻.

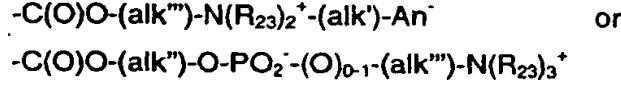
[0093] Suitable cationic groups of the moiety Zw are for example a group -NR₂₃R₂₃'R₂₃"⁺ or a bivalent group -NR₂₃R₂₃"⁺, wherein R₂₃, R₂₃' and R₂₃" are as defined above, and are each independently of the other, preferably hydrogen or C₁-C₆-alkyl, preferably hydrogen or C₁-C₄-alkyl and most preferably each methyl or ethyl.

[0094] The moiety Zw is for example C₂-C₃₀-alkyl, preferably C₂-C₁₂-alkyl, and more preferably C₃-C₈-alkyl, which is in each case uninterrupted or interrupted by -O- and substituted or interrupted by one of the above-mentioned anionic and cationic groups each, and, in addition, is further unsubstituted or substituted by a radical -OY₈, wherein Y₈ is hydrogen or the acyl radical of a carboxylic acid.

[0095] Y₈ is preferably hydrogen or the acyl radical of a higher fatty acid.

[0096] Zw is preferably C₂-C₁₂-alkyl and even more preferably C₃-C₈-alkyl which is substituted or interrupted by one of the above-mentioned anionic and cationic groups each, and in addition may be further substituted by a radical -OY₈.

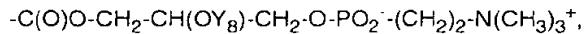
[0097] A preferred group of zwitter-ionic substituents -R₂₄-Zw corresponds to the formula



50 wherein R₂₃ is hydrogen or C₁-C₆-alkyl; An⁻ is an anionic group -COO⁻, -SO₃⁻, -OSO₃⁻ or -OPO₃H⁻, preferably -COO⁻ or -SO₃⁻ and most preferably -SO₃⁻, alk' is C₁-C₁₂-alkylene, (alk") is C₂-C₂₄-alkylene which is unsubstituted or substituted by a radical -OY₈, Y₈ is hydrogen or the acyl radical of a carboxylic acid, and (alk") is C₂-C₈-alkylene.

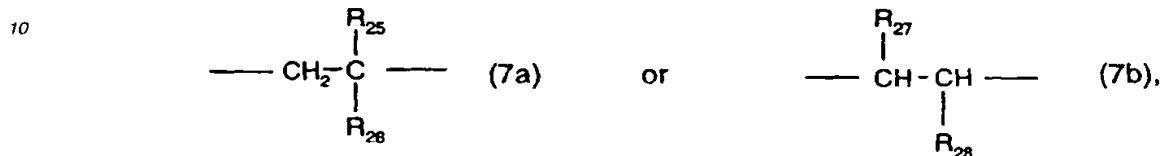
[0098] (alk') is preferably C₂-C₈-alkylene, more preferably C₂-C₆-alkylene and most preferably C₂-C₄-alkylene. (alk") is preferably C₂-C₁₂-alkylene, more preferably C₂-C₆-alkylene and particularly preferably C₂-C₃-alkylene which is in each case unsubstituted or substituted by hydroxy or by a radical -OY₈. (alk") is preferably C₂-C₄-alkylene and more preferably C₂-C₃-alkylene. R₉ is hydrogen or C₁-C₄-alkyl, more preferably methyl or ethyl and particularly preferably

methyl. A preferred zwitterionic substituent of B or B' is of formula



5 wherein Y₈ is hydrogen or the acyl radical of a higher fatty acid.

[0099] B denotes for example a radical of formula

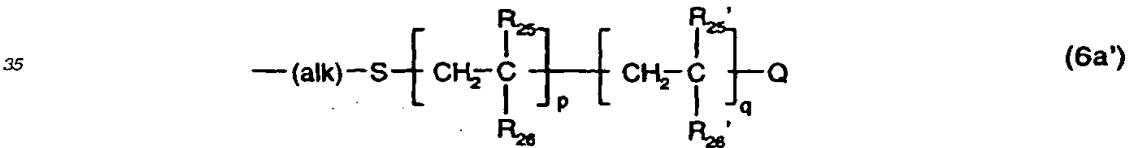


20 wherein R₂₅ is hydrogen or C₁-C₄-alkyl, preferably hydrogen or methyl; R₂₆ is a hydrophilic substituent, wherein the above given meanings and preferences apply; R₂₇ is C₁-C₄-alkyl, phenyl or a radical -C(O)OY₉, wherein Y₉ is hydrogen or unsubstituted or hydroxy-substituted C₁-C₄-alkyl; and R₂₈ is a radical -C(O)Y₉' or -CH₂-C(O)OY₉', wherein Y₉' independently has the meaning of Y₉.

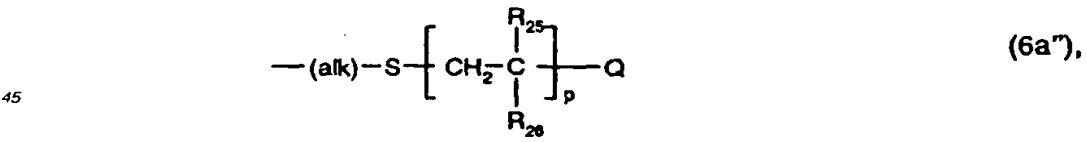
25 [0100] R₂₇ is preferably C₁-C₂-alkyl, phenyl or a group -C(O)OY₉. R₂₈ is preferably a group -C(O)OY₉' or -CH₂-C(O)OY₉', wherein Y₉ and Y₉' are each independently of the other hydrogen, C₁-C₂-alkyl or hydroxy-C₁-C₂-alkyl. Particularly preferred -CHR₂₇-CHR₂₈- units according to the invention are those wherein R₂₇ is methyl or a group -C(O)OY₉ and R₂₈ is a group -C(O)OY₉' or -CH₂-C(O)OY₉', wherein Y₉ and Y₉' are each hydrogen, C₁-C₂-alkyl or hydroxy-C₁-C₂-alkyl.

[0101] B' independently may have one of the meanings given above for B.

30 [0102] If (oligomer) is a radical of formula (6a), the radical -(alk)-S-[B]_p-[B']_q-Q preferably denotes a radical of formula

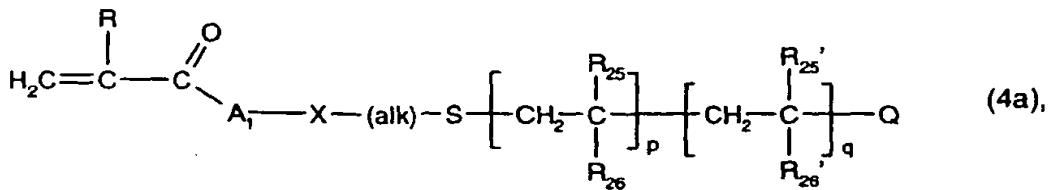


40 and even more preferably of the formula



50 wherein for R₂₅, R₂₆, Q, p and q the above-given meanings and preferences apply, for R₂₅' independently the meanings and preferences given before for R₂₅ apply, and for R₂₆' independently the meanings and preferences given before for R₂₆ apply.

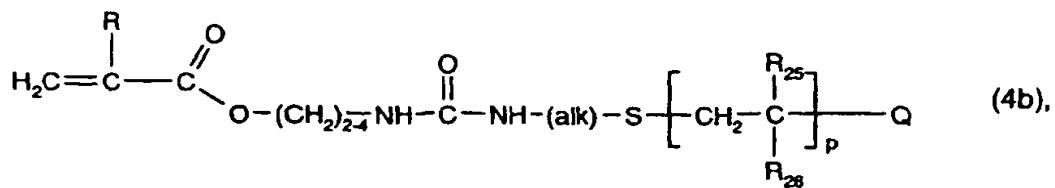
55 [0103] A preferred group of suitable hydrophilic macromonomers according to step (b) of the invention comprises compounds of formula



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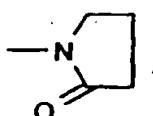
wherein R is hydrogen or methyl, A₁ is -O-(CH₂)₂₋₄-, -O-CH₂-CH(OH)-CH₂- or a radical -O-(CH₂)₂₋₄-NH-C(O)-, X is -O- or -NH-, (alk) is C₂-C₄-alkylene, Q is a monovalent group that is suitable to act as a polymerization chain-reaction terminator, p is an integer from 5 to 50, R₂₅ and R_{25'} are each independently of the other hydrogen or methyl, and for R₂₆ and R_{26'} each independently the above given meanings and preferences apply.

[0104] A particularly preferred embodiment of the invention relates to hydrophilic macromonomers of the formula



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wherein for R, R₂₅, R₂₆, Q, (alk) and p the above-given meanings and preferences apply. A particularly preferred group of hydrophilic macromonomers are compounds of the above formula (4b) wherein R is hydrogen or methyl, (alk) is C₂-C₄-alkylene, R₂₅ is hydrogen or methyl, p is an integer of 5 to 50, Q is as defined before, and for R₂₆ the above given meanings and preferences apply; in particular R₂₆ of this embodiment is a radical -CONH₂, -CON(CH₃)₂ or



45 [0105] If (oligomer) is a radical (ii) of formula (6b), Q' in formula (6b) is for example C₁-C₁₂-alkyl, phenyl or benzyl, preferably C₁-C₂-alkyl or benzyl and in particular methyl. R₁₉ is preferably unsubstituted or hydroxy-substituted C₁-C₄-alkyl and in particular methyl. u is preferably an integer from 2 to 150, more preferably from 5 to 100, even more preferably from 5 to 75 and particularly preferably from 10 to 50.

[0106] If (oligomer) is a radical of formula (6b'), the above given meanings and preferences apply for the variables R₁₉ and u contained therein. X in formula (6b') is preferably hydroxy or amino.

[0107] If (oligomer) denotes a radical (iv) of formula (6c), R₂₀ and R_{20'} are each preferably ethyl or in particular methyl; v is preferably an integer from 2 to 150, more preferably from 5 to 100, even more preferably from 5 to 75 and particularly preferably from 10 to 50; Q" is for example hydrogen; and An⁻ is as defined before.

[0108] If (oligomer) denotes an oligopeptide radical (v) of formula (6d) or 6d'), R₂₁ is for example hydrogen, methyl, hydroxymethyl, carboxymethyl, 1-hydroxyethyl, 2-carboxyethyl, isopropyl, n-, sec. or iso-butyl, 4-amino-n-butyl, benzyl, p-hydroxybenzyl, imidazolylmethyl, indolylmethyl or a radical -(CH₂)₃-NH-C(=NH)-NH₂. t is preferably an integer from 2 to 150, more preferably from 5 to 100, even more preferably from 5 to 75 and particularly preferably from 10 to 50.

[0109] If (oligomer) denotes a polyoxyalkylene radical (vi) of formula (6e), R₃₄ is preferably hydrogen or C₁-C₁₈-

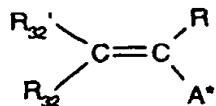
alkyl, more preferably hydrogen or C₁-C₁₂-alkyl, even more preferably hydrogen, methyl or ethyl, and particularly preferably hydrogen or methyl. (alk**) is preferably a C₂-C₃-alkylene radical. z is preferably 0. r and s are each independently preferably an integer from 0 to 100 wherein the total of (r+s) is 5 to 100. r and s are each independently more preferably an integer from 0 to 50 wherein the total of (r+s) is 8 to 50. In a particularly preferred embodiment of the polyoxyalkylene radicals (oligomer), r is an integer from 8 to 50 and particularly 9 to 25, and s is 0.

[0110] (oligomer) as the radical of an oligosaccharide (vii) may be, for example, a di- or polysaccharide including carbohydrate containing fragments from a biopolymer. Examples are the radical of a cyclodextrin, trehalose, cellobiose, maltotriose, maltohexaose, chitohexaose or a starch, hyaluronic acid, deacetylated hyaluronic acid, chitosan, agarose, chitin 50, amylose, glucan, heparin, xylan, pectin, galactan, glycosaminoglycan, mucin, dextran, aminated dextran, cellulose, hydroxylalkylcellulose or carboxyalkylcellulose oligomer, each of which with a molecular weight average weight of, for example, up to 25000, preferably up to 10000. Preferably the oligosaccharide according to (vii) is the radical of a cyclodextrin with a maximum of 8 sugar units.

[0111] Formulae (6a), (6a') or (6e) are to be understood as a statistic description of the respective oligomeric radicals, that is to say, the orientation of the monomers and the sequence of the monomers (in case of copolymers) are not fixed in any way by said formulae. The arrangement of B and B' in formula (6a) or of the ethyleneoxide and propyleneoxide units in formula (6e) thus in each case may be random or blockwise.

[0112] The weight average molecular weight of the hydrophilic macromonomer according to step (b) depends principally on the desired properties and is for example from 300 to 25000, preferably from 300 to 12000, more preferably from 300 to 8000, even more preferably from 300 to 5000, and particularly preferably from 500 to 4000.

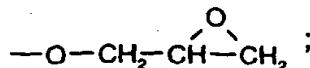
[0113] The macromonomers of formula (4) may be prepared by methods known per se. For example, the compounds of formula (4) wherein A is a radical of formula (5a), (5b) or (5d) are obtainable by reacting a compound of formula



(8)

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wherein R, R₃₂ and R₃₂' each have the above-given meaning and A* is, for example, a group -C(O)-A**, wherein A** is halogen, particularly chlorine, an ester group an oxyalkylene radical comprising an epoxy group, for example the radical



40

or is a radical -O-C₂-C₁₂-alkylene-N=C=O; or A* is a radical -(A₂)_m-N=C=O, wherein A₂ and m have the above-given meaning, with a compound of formula



(9),

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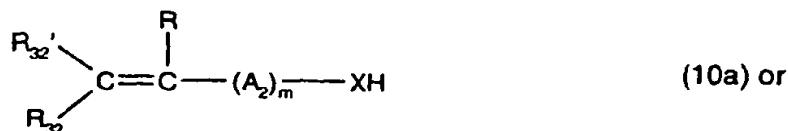
wherein X has the above-given meaning.

[0114] The reactions of a compound of formula (8) having a carboxylic acid halide group, an epoxy group or an isocyanato group with an amino or hydroxy compound of formula (9) are well-known in the art and may be carried out as described in textbooks of organic chemistry. For example, the reaction of an isocyanato derivative of formula (8) with a compound of formula (9) may be carried out in an inert organic solvent such as an optionally halogenated hydrocarbon, for example petroleum ether, methylcyclohexane, toluene, chloroform, methylene chloride and the like, or an ether, for example diethyl ether, tetrahydrofuran, dioxane, or a more polar solvent such as DMSO, DMA, N-methylpyrrolidone or even a lower alcohol, at a temperature of from 0 to 100°C, preferably from 0 to 50°C and particularly preferably at room temperature, optionally in the presence of a catalyst, for example a tertiary amine such as triethylamine or tri-n-butylamine, 1,4-diazabicyclooctane, or a tin compound such as dibutyltin dilaurate or tin dioctanoate. In addition, the reaction of an isocyanato derivative of formula (8) with a compound of formula (9) wherein -XH is an amino group also may be carried out in an aqueous solution in the absence of a catalyst. It is advantageous to carry out the above reac-

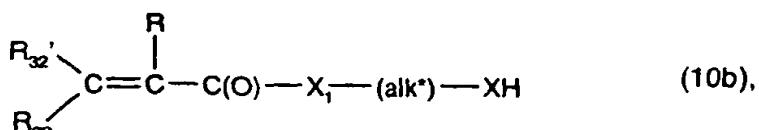
tions under an inert atmosphere, for example under an nitrogen or argon atmosphere.

[0115] Moreover, the macromonomers of formula (4) wherein A is a radical of formula (5c) or (5e) may be obtained by reacting a compound of formula

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20 wherein R, R₃₂, R_{32'}, A₂, X, X₁, (alk*) and m each have the above-given meaning, with a compound of formula

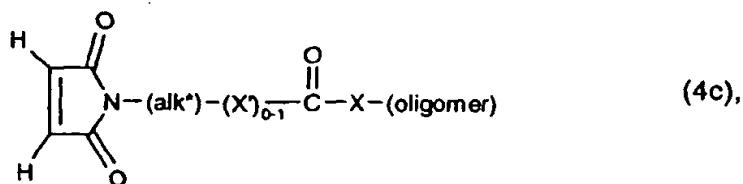


25 wherein (oligomer) has the above-given meaning and X₁' is for example -OH or halogen, in particular chlorine, or together with -(O)C- forms an anhydride group, in a manner known per se.

[0116] The macromonomers of formula (4), wherein A is a direct bond and (oligomer) is a radical of formula (6c') are known or may be prepared according to methods known in the art, for example as described in S. Kobayashi et al., Polymer Bulletin 13, p 447-451 (1985).

30 [0117] Likewise, the macromonomers of the formula

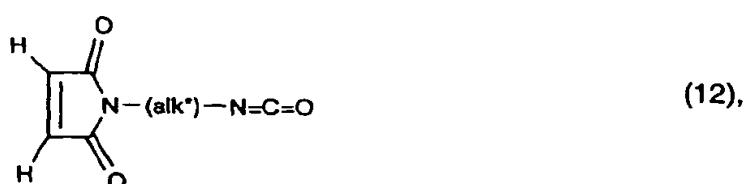
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wherein (alk*), X', X and (oligomer) each have the above-given meaning, may be obtained in a manner known per se, for example, by reacting a compound of formula

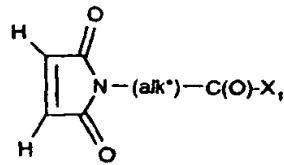
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wherein (alk*) has the above-given meaning, with a compound of the above-given formula (6), or by reacting a compound of formula



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with a compound of the above formula (9) wherein (alk*) and X₁ each have the above-given meaning.

[0118] The compounds of the formula (8), (9), (9a), (10a), (10b), (12) and (12a) are known compounds which are commercially available or may be prepared according to known methods. For example, compounds of the formula (9) and (9a) wherein (oligomer) denotes a radical of formula (6a) may be prepared according to PCT application WO 92/09639 by copolymerizing one or more hydrophilic ethylenically unsaturated monomers in the presence of a functional chain transfer agent such as cysteamine hydrochloride, thioglycolic acid or the like.

[0119] The hydrophilic monomers or macromonomers may be applied to the initiator-modified primary polymer coating and polymerized there according to processes known per se. For example, the material comprising the primary polymer coating is immersed in a solution of the monomer or macromonomer, or a layer of monomer or macromonomer is first of all deposited on the modified material surface, for example, by dipping, spraying, spreading, knife coating, pouring, rolling, spin coating or vacuum vapor deposition. Suitable solvents, if used in the polymerization process, are, for example, water or dipolar aprotic solvents such as, for example, acetonitrile. The polymerization of the hydrophilic monomer or macromonomer on the material comprising the primary polymer coating then may be initiated, for example, thermally by the action of heat or preferably by irradiation, particularly by UV radiation. Suitable light sources for the irradiation are known to the artisan and comprise for example mercury lamps, high pressure mercury lamps, xenon lamps, carbon arc lamps or sunlight. The time period of irradiation may depend for example on the desired properties of the resulting composite material but is usually in the range of up to 30 minutes, preferably from 10 seconds to 10 minutes, and particularly preferably from 0.5 to 5 minutes. It is advantageous to carry out the irradiation in an atmosphere of inert gas. After the polymerization, any non-covalently bound monomers, polymers, oligomers or non-reacted macromonomers formed can be removed, for example by treatment with suitable solvents.

[0120] The coated material obtained according to the invention may be purified afterwards in a manner known per se, for example by washing or extraction with a suitable solvent such as water.

[0121] According to step (b) of the above-described coating process, the brushes of the primary coating obtained according to step (a) are provided with side chains by grafting a hydrophilic monomer or macromonomer onto the primary polymer coating. The final coating typically has a so-called bottle brush-type structure (BBT) composed of tethered "hairy" chains. The BBT structure of the coatings of the invention may be varied within wide limits, for example by a suitable choice of reactive monomer, photoinitiator and chain length in step (a), or by a suitable choice of hydrophilic monomer or macromonomer and chain length in step (b). Such BBT structures in one embodiment comprise a long hydrophilic or hydrophobic backbone which carries relatively densely packed comparatively short hydrophilic side chains (called primary bottle brushes). Another embodiment relates to secondary bottle brushes which are characterized in that the hydrophilic side chains themselves carry densely packed hydrophilic "secondary" side chains. Polymeric coatings of said primary and secondary BBT structures to a certain extent mimic highly water-retaining structures occurring in the human body, for example in cartilage or mucosal tissue.

[0122] The coating thickness of the macromonomers depends principally on the desired properties. It can be, for example, from 0.001 to 1000 µm, preferably from 0.005 to 100 µm, more preferably from 0.01 to 50 µm, even more preferably from 0.01 to 5 µm, especially preferably from 0.01 to 1 µm and particularly preferably from 0.01 to 0.5 µm.

[0123] A further embodiment of the invention relates to a material that is coated by the process of the invention.

[0124] The material that is coated by the process of the invention is, for example, an organic bulk material, preferably a biomedical device, e.g. an ophthalmic device, preferably a contact lens including both hard and particularly soft contact lenses, an intraocular lens or artificial cornea. Further examples are materials useful for example as wound healing dressings, eye bandages, materials for the sustained release of an active compound such as a drug delivery patch, moldings that can be used in surgery, such as heart valves, vascular grafts, catheters, artificial organs, encapsulated biologic implants, e.g. pancreatic islets, materials for prostheses such as bone substitutes, or moldings for diagnostics, membranes or biomedical instruments or apparatus.

[0125] The biomedical devices, e.g. ophthalmic devices obtained according to the invention have a variety of unexpected advantages over those of the prior art which make those devices very suitable for practical purposes, e.g. as con-

tact lens for extended wear or intraocular lens. For example, they do have a high surface wettability which can be demonstrated by their contact angles, their water retention and their water-film break up time or tear film break up time (TBUT).

[0126] The TBUT plays an particularly important role in the field of ophthalmic devices such as contact lenses.

5 Thus the facile movement of an eyelid over a contact lens has proven important for the comfort of the wearer; this sliding motion is facilitated by the presence of a continuous layer of tear fluid on the contact lens, a layer which lubricates the tissue/lens interface. However, clinical tests have shown that currently available contact lenses partially dry out between blinks, thus increasing friction between eyelid and the lens. The increased friction results in soreness of the eyes and reduced movement of the contact lenses. Now it has become feasible to considerably increase the TBUT of commercial 10 contact lenses such as, for example, Focus Dailies™, Focus New Vues® or Lotrafilcon A lenses, by applying a surface coating according to the invention. On the base curve of a contact lens, the pronounced lubricity of the coating facilitates the on-eye lens movement which is essential for extended wear of contact lenses. Moreover, the materials obtained by the process of the invention provide additional effects being essential for lenses for extended wear, such as an increased thickness of the pre-lens tear film which contributes substantially to low microbial adhesion and resistance to 15 deposit formation. Due to the extremely soft and lubricious character of the novel surface coatings, biomedical articles such as in particular contact lenses coated by the process of the invention show a superior wearing comfort including improvements with respect to late day dryness and long term (overnight) wear. The novel surface coatings moreover interact in a reversible manner with ocular mucus which contributes to the improved wearing comfort.

[0127] In addition, biomedical devices, e.g. ophthalmic devices such as contact lenses, coated by the process of

20 the invention, have a very pronounced biocompatibility combined with good mechanical properties. For example, the devices are blood compatible and have a good tissue integration. In addition, there are generally no adverse eye effects observed, while the adsorption of proteins or lipids is low, also the salt deposit formation is lower than with conventional contact lenses. Generally, there is low fouling, low microbial adhesion and low bioerosion while good mechanical properties can be for example found in a low friction coefficient and low abrasion properties. Moreover, the dimensional 25 stability of the materials obtained according to the invention is excellent. In addition, the attachment of a hydrophilic surface coating at a given bulk material according to the invention does not affect its visual transparency.

[0128] In summary, the ophthalmic devices obtained by the process of the invention, such as contact lenses and

30 artificial cornea, provide a combination of low spoilage with respect to cell debris, cosmetics, dust or dirt, solvent vapors or chemicals, with a high comfort for the patient wearing such ophthalmic devices in view of the soft hydrogel surface which for example provides a very good on-eye movement of the ophthalmic device.

[0129] Biomedical devices such as renal dialysis membranes, blood storage bags, pacemaker leads or vascular grafts coated by the process of the invention resist fouling by proteins by virtue of the continuous layer of bound water, thus reducing the rate and extent of thrombosis. Blood-contacting devices fabricated according to the present invention are therefore haemocompatible and biocompatible.

35 [0130] In the examples, if not indicated otherwise, amounts are amounts by weight, temperatures are given in degrees Celsius. Tear break-up time values in general relate to the pre-lens tear film non-invasive break-up time (PLTF-NIBUT) that is determined following the procedure published by M. Guillot et al., *Ophthal. Physiol. Opt.* **9**, 355-359 (1989) or M. Guillot et al., *Optometry and Vision Science* **74**, 273-279 (1997). Average advancing and receding water contact angles of coated and non-coated lenses are determined with the dynamic Wilhelmy method using a Krüss K-40 12 instrument (Krüss GmbH, Hamburg, Germany). Wetting force on the solid is measured as the solid is immersed in or withdrawn from a liquid of known surface tension.

Surface functionalization

45 **Example A-1: 1,2-Diaminocyclohexane plasma coating (DACH)**

[0131] Two dried Lotrafilcon A lenses (polysiloxane/perfluoroalkyl polyether copolymer) are, after extraction in isopropanol, toluene and again in isopropanol, placed on the glass holder within the plasma reactor equipped with an external ring electrode and a 27.13 MHz radiofrequency (RF) generator for the generation of an inductively-coupled,

50 cold glow discharge plasma. The distance between the substrates and the lower edge of the plasma zone is 12 cm. The reactor is evacuated to a pressure of 0.008 mbar, and held at these conditions for one hour. Then, the argon plasma gas flow rate into the plasma zone of the reactor is set to 20 sccm (standard cubic centimeter), the pressure in the reactor is adjusted to 0.12 mbar and the RF generator is switched on. The plasma discharge of a power 250 Watts is maintained for a total period of 1 min (in order to clean and activate the lenses surfaces). Afterward the 1,2-DACH vapor is 55 introduced into the reactor chamber from DACH reservoir (maintained at 24 °C) at 0.15 mbar for 1 min. After this, the following parameters for the plasma polymerization of DACH are chosen : Argon flow rate for plasma excitation = 5 sccm, Argon carrier gas flow rate for DACH transport = 5 sccm, temperature of the DACH evaporation unit = 24 °C, the distance between the lower edge of the plasma zone and the substrates = 5 cm, pressure = 0.2 mbar, and plasma

power = 100 W. The lenses are treated for about 5 minutes with a pulsing glow discharge plasma (1 μ sec. on, 3 μ sec. off). After 5 minutes of deposition the plasma discharge is interrupted and DACH vapor is let to flow into reactor for other 5 min. The reactor is then evacuated and maintained for 30 minutes at a pressure 0.008 mbar in order to remove residual monomer and activated species. The internal pressure is brought to atmospheric by using dry nitrogen. The substrates are then turned over and the whole procedure is repeated to coat the other side of the substrates. The samples are then unloaded from the reactor and used for the subsequent photoinitiator linkage.

Example A-2: Surface binding of a reactive photoinitiator

10 [0132] The aminofunctionalized contact lenses from Example A-1 are, immediately after plasma treatment with 1,2-DACH plasma, immersed into 1 % acetonitrile solution of the reactive photoinitiator (I) prepared by the addition reaction from Isophorone diisocyanate and 4-(2-hydroxyethoxy)phenyl 2-hydroxy-2-propyl ketone (Darocure 2959) by the method described in EP 0 632 329. The amino groups on the lenses surfaces react with the isocyanato groups of the photoinitiator molecules for 12 hours. After this time, the lenses are withdrawn from the reaction solution, washed and extracted in acetonitrile for 8 hours and dried under reduced pressure for 2 hours. The dried lenses are subsequently used for photografting.

Example A-3: Surface binding of a reactive photoinitiator

20 [0133] The aminofunctionalized contact lenses from Example A-1 are, immediately after plasma treatment with 1,2-DACH plasma, immersed into 1 % acetonitrile solution of the reactive photoinitiator (II) prepared by the addition reaction from Isophorone diisocyanate and 2-ethyl-2-(dimethylamino)-1-[4-(2-hydroxyethoxy)phenyl]-4-penten-1-one by the method described in WO 96/20796. The amino groups on the lenses surfaces react with the isocyanato groups of the photoinitiator molecules for 16 hours. After this time, the lenses are withdrawn from the reaction solution, washed and extracted in acetonitrile for 12 hours and dried under reduced pressure for 2 hours. The dried lenses are subsequently used for photografting.

Example A-4: Surface binding of a thermal polymerization initiator

30 [0134] 1 g of the reactive initiator 4,4'-Azobis(4-cyanovaleic acid) (ACV), 25 ml of anhydrous Acetonitrile and 0.5 g of N,N'-Dicyclohexylcarbodiimide (DCC) are charged into a 100 ml flask with a flat bottom. The mixture is stirred under nitrogen at 25 °C for 10 minutes. The aminofunctionalized contact lenses from Example A-1 are then separately immersed into the solution. The reaction between activated carboxylic groups of ACV and amino groups on lens surfaces proceeds under nitrogen at RT for 16 hours. After the reaction, the lenses are withdrawn from the reaction solution, washed and extracted in acetonitrile for 12 hours and dried under reduced pressure for 2 hours.

Photografting of reactive monomers

Example B-1: Photografting of 2-isocyanatoethyl methacrylate (IEM) onto the contact lens surface

40 [0135] 1.0 g of IEM is dissolved in 9 ml of acetonitrile and the solution is stirred under argon flow for 5 minutes. Argon is then let to bubble through the solution for the period of about 10 minutes. The solution is then filtered through 0.45 μ m Teflon filter and degassed with argon for additional 10 minutes. The filtered solution is then frozen in a flask in liquid nitrogen, the flask is evacuated under a high vacuum, transferred into a glove box and used for photografting.

45 1 ml of the IEM solution is introduced into a small Petri dish of a volume of about 3 ml in a glow box. The dried lens from Example A-2, carrying covalently linked photoinitiator molecules on its surface, is then placed into this solution and an additional 1 ml of the degassed solution is added on the lens in order to cover the whole lens with the solution. After 5 minutes, the Petri dish with the lens in the solution is exposed to 15 mW ultraviolet light for a period of about 3 minutes. The lens is then turned over and the exposition is repeated by applying 15 mW UV light for an additional 3 minutes.

50 The modified lens is then withdrawn from the solution, washed twice in dried acetonitrile, continuously extracted and dried acetonitrile for 2 h.

Example B-2: Photografting of 2-vinyl-4,4-dimethyl azlactone (VAL) onto the contact lens surface

55 [0136] 1.5 g of VAL are dissolved in 13.5 ml of acetonitrile and the solution is stirred under argon flow for 5 minutes. Argon is then let to bubble through the solution for the period of about 10 minutes. The solution is then filtered through 0.45 μ m Teflon filter and degassed with argon for additional 10 minutes. The filtered solution is then frozen in a flask in liquid nitrogen, the flask is evacuated under a high vacuum, transferred into a glove box and used for photografting.

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1 ml of the VAL solution is introduced into a small Petri dish of a volume of about 3 ml in a glove box. The dried lens from Example A-3, carrying covalently linked photoinitiator molecules on its surface, is then placed into this solution and an additional 1 ml of the degassed solution is added on the lens in order to cover the whole lens with the solution. After 5 minutes, the Petri dish with the lens in the solution is exposed to 15 mW ultraviolet light for a period of about 3 minutes. 5 The lens is then turned over and the exposition was repeated by applying 15 mW UV light for an additional 3 minutes. The modified lens is then withdrawn from the solution, washed twice in dried acetonitrile and continuously extracted in dried acetonitrile for 2 h.

Examples B-3 to B-5: Photografting of other reactive molecules onto the contact lens surface

10 [0137] The following reactive monomers are photografted onto the lens surface obtained according to Example A-2 using the process described in Examples B-1 and B-2:

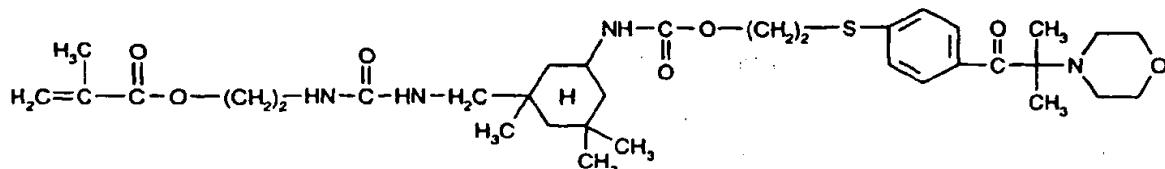
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Example	Monomer used
B-3	Glycidyl methacrylate
B-4	Acrylic acid
B-5	Acrylic acid anhydride

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Example B-6: Thermografting of a polymerizable photoinitiator onto the contact lens surface

25 [0138] A 100 ml flask with a flat bottom, condenser and thermometer is charged with 1.5 g of the polymerizable photoinitiator of the formula



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(synthesis see PCT application WO 96/20919, Example H1 on page 53) and 13.5 ml of acetonitrile and the solution is stirred under argon flow for 5 minutes. Argon is then let to bubble through the solution for the period of about 10 minutes. The solution is then filtered through 0.45 µm Teflon filter and degassed with argon for additional 10 minutes. The dried lenses from Example A-4, carrying covalently linked initiator molecules on its surface, are then placed into the solution.

40 The whole mixture is then heated to 60 °C to start the polymerization process. Polymerization proceeds under argon flow and gentle stirring of the mixture, at 60 °C for 24 hours. The modified lenses are then withdrawn from the solution, washed twice in anhydrous acetonitrile, continuously extracted in anhydrous acetonitrile for additional 4 h and used for further modification.

45 Introduction of polymerization initiators to the primary polymer coating

Example C-1: Coupling of 4-(2-hydroxyethoxy)phenyl 2-hydroxy-2-propyl ketone (Darocure 2959) to isocyanate groups of poly-IEM chains grafted on a lens surface

50 [0139] The isocyanate groups of the functionalized lens from Example B-1 are reacted with 4-(2-hydroxyethoxy)phenyl 2-hydroxy-2-propyl ketone (Darocure 2959) by immersing the lens into 3 ml acetonitrile solution containing 30 mg of Darocure 2959 and 10 µg of dibutyltin dilaurate (DBTDL) as catalyst. The reaction is carried out under argon atmosphere at 30 °C for 48 hours. The lens is then withdrawn from the solution, washed 2x in acetonitrile, continuously extracted in acetonitrile for 4 hours, dried and used for photografting.

55

Example C-2: Coupling of δ,δ' -azo-bis(δ -cyano-n-pentanol) to isocyanate groups of poly-IEM chains grafted on a lens surface

5 [0140] The coupling of δ,δ' -azo-bis(δ -cyano-n-pentanol) to isocyanate groups of the functionalized lens from Example B-1 is done analogously to Example C-1.

Synthesis of telomers and macromonomers

Example D-1: Acrylamide telomer

10 [0141] A 1000 mL three-necked round bottom flask is charged with a solution of 17.5 g (154 mmol) cysteamine hydrochloride in 150 deionized water. 1.1 g (4 mmol) α,α' -azodiisobutyramidine dihydrochloride and a solution of 142 g (2 mol) acrylamide in 450 mL deionized water are added. The pH of the solution is adjusted to pH 3 by addition of 1 molar hydrochloric acid. An intensive cooler and an internal thermometer are connected to the flask. The apparatus is 15 evacuated to 100 mbar and filled with argon. This is repeated five times. The mixture is heated to 60°C for three hours and then cooled to room temperature. An analytical sample is freeze-dried and the monomer conversion was determined by $^1\text{H-NMR}$ spectroscopy. No resonances corresponding to C=C double bonds can be detected, indicating >98 % conversion of the monomer.

20 The pH of the remaining mixture is adjusted to 10.5 by addition of 1 molar sodium hydroxide solution and diluted to a total volume of 1200 mL. Salts and low molecular weight residues such as unreacted chain transfer agent are removed by reverse osmosis using a Millipore Proscale system equipped with a Millipore Helicon RO-4 Nanomax 50 membrane operating at a pressure of 15 bar. The product is isolated from the obtained retentate by freeze-drying. Yield: 102 g of a white powder.

25 The concentration of amino groups is determined by functional group titration, result 0.22 mmol/g NH₂ corresponding to an average molecular weight of the telomer of 4500 g/mol. GPC-analysis indicate a monomodal molecular weight distribution and the absence of high molecular weight polymer.

Example D-2: Acryloyl morpholine telomer

30 [0142] A 100 mL three-necked round bottom flask is charged with a solution of 1.6 g (14.3 mmol) cysteamine hydrochloride in 45 mL of 0.1 molar aqueous acetic acid. 55 mg (0.2 mmol) α,α' -azodiisobutyramidine dihydrochloride and 14.1 g (100 mmol) acryloyl morpholine are added. An intensive cooler and an internal thermometer are connected to the flask. The apparatus is evacuated to 100 mbar and filled with argon. This is repeated five times. The mixture is heated to 60°C for four hours and then cooled to room temperature. An analytical sample is freeze-dried and the monomer conversion is determined by $^1\text{H-NMR}$ spectroscopy. No resonances corresponding to C=C double bonds can be detected, indicating >98 % conversion of the monomer.

The remaining mixture is freeze-dried, dissolved in methanol and the telomer is precipitated in 2 liters of diethyl ether and collected by filtration.

35 [0143] The telomer is redissolved in 50 mL water and the pH is adjusted to 10.5 by addition of 143 mL 0.1 molar sodium hydroxide solution and then diluted with water to a total volume of 500 mL. Salts and residual low molecular weight components are removed by ultrafiltration using a UFP-1-E-4A cartridge from A/G Technology Corporation, Needham, MA. The concentration of amino-groups is determined by functional group titration, result 0.54 mmol/g NH₂ corresponding to an average molecular weight of the telomer of 1850 g/mol.

45 **Example D-3:** Telomer from α,α' -mono- isocyanatoethyl methacrylato trehalose

[0144] A 100 mL three-necked round bottom flask is charged with a solution of 3.8 g (33.4 mmol) cysteamine hydrochloride in 45 mL of 0.1 molar aqueous acetic acid. 55 mg (0.2 mmol) α,α' -azodiisobutyramidine dihydrochloride and 53 g (106 mmol) mono-isocyanatoethyl methacrylato trehalose are added. An intensive cooler and an internal thermometer are connected to the flask. The apparatus is evacuated to 100 mbar and filled with argon. This is repeated five times. The mixture is heated overnight to 60°C and then cooled to room temperature. The product precipitates in 2 liters of acetone and is isolated by filtration, yielding a slightly yellow colored powder. No resonances corresponding to C=C double bonds can be detected by $^1\text{H-NMR}$ spectroscopy, indicating >98 % conversion of the monomer.

50 The product is dissolved in 200 mL water and the pH is adjusted to 10.5 by addition of 107 mL 0.1 molar sodium hydroxide solution and then diluted with water to a total volume of 500 mL. Salts and residual low molecular weight components are removed by ultrafiltration using a UFP-1-E-4A cartridge from A/G Technology Corporation, Needham, MA. The concentration of amino-groups is determined by functional group titration, result 0.12 mmol/g NH₂ corresponding to an average molecular weight of the telomer of 8300 g/mol and a degree of polymerization of 16.

Example D-4: Co-telomerization of hydroxyethyl acrylamide and N-acryloyl morpholine

[0145] A 1000 mL three-necked round bottom flask is charged with a solution of 28.4 g (250 mmol) cysteamine hydrochloride in 400 mL deionized water. 407 mg (1.5 mmol) α,α' -azodiisobutyramidine dihydrochloride and 70.6 g (500 mmol) acryloyl morpholine and 28.8 g (250 mmol) N-hydroxyethyl acrylamide are added. An intensive cooler and an internal thermometer are connected to the flask. The apparatus is evacuated to 100 mbar and filled with argon. This

5 is repeated five times. The mixture is heated to 60°C for four hours and then cooled to room temperature. An analytical sample is freeze-dried and the monomer conversion is determined by $^1\text{H-NMR}$ spectroscopy. No resonances corresponding to C=C double bonds can be detected, indicating >98 % conversion of the monomer.

10 The remaining mixture is adjusted to pH = 10 by addition of 30% KOH solution. Salts and low molecular weight residues such as unreacted chain transfer agent are removed by reverse osmosis using a Millipore Proscale system equipped with a Millipore Helicon RO-4 Nanomax 50 membrane operating at a pressure of 15 bar. The product is isolated from the obtained retentate by freeze-drying.

15 The concentration of amino-groups is determined by functional group titration, result 0.95 mmol/g NH_2 corresponding to an average molecular weight of the co-telomer of 1050 g/mol. GPC-analysis indicates a monomodal molecular weight distribution and the absence of high molecular weight polymer.

Example D-5: Acrylamide telomer

20 [0146] A 1000 mL round bottom flask is charged with a solution of 71.1g (1 mol) acrylamide, 4.93g (18.2 mmol) α,α' -azodiisobutyramidine dihydrochloride and 4.93 g (36.4 mmol) Cysteaminhydrochloride in 400 mL of water. The clear and slightly yellowish solution is acidified with a few drops of Hydrochloric Acid to pH3. The stirred acidic solution is evacuated to 50 mbar and filled with argon. This is repeated three times. With a constant stream of Argon, this solution is poured into a 500 ml dropping funnel which was put onto a 'flow-through-reactor' consisting of a 1000mL three-necked round-bottom flask, reflux condenser, thermometer, magnetic stirrer and a 30 cm Liebig-condenser, which is filled with glass wool. The whole apparatus is constantly purged with Argon.

The dropping funnel is put onto the Liebig condenser, which is heated to 65°C. The flask is heated to 60°C. Slowly the solution is dropped through the Liebig—condenser into the stirred flask. This takes 2.5 hrs in which the temperature in the flask is kept between 58–65°C. After the completion of the addition, the solution is stirred for 2hrs at 60°C.

30 NaOH is added to the clear and slightly yellowish solution until pH10 is reached. The product is cleaned through reverse osmosis, using Millipore cartridge with a cut-off at 1000 Da and freeze-dried. A bright-white solid product is obtained. The concentration of amino groups is determined via functional group titration (0.34mEq/g) which corresponds well with the sulfur-value of the elemental analysis (0.33mEq/g). M_n 2000g/Mol.

Example D-6: Preparation of an acrylamide macromonomer

35 [0147] 6.5 g of the acrylamide telomer with an amino end group (amine titration = 0.22 mEq/g), prepared according to Example D-1 are dissolved in 80 ml of 0.15 M aqueous NaCl. Argon is then let to bubble through the solution for the period of about 30 minutes. This mixture is then added to the equimolar amount (0.2 g) of isocyanatoethyl methacrylate (IEM, isocyanate titration = 6.45 mEq/g) under stirring. The whole mixture is then stirred under argon flow for 4 hours. The mixture is then filtered through 0.45 μm Teflon filter, degassed with argon in order to remove oxygen and used for photografting.

Example D-7: Preparation of an acryloylmorpholine macromonomer

45 [0148] 6.2 g of the acryloylmorpholine telomer with an amino end group (amine titration = 0.54 mEq/g), prepared according to Example D-2 are dissolved in 80 ml of HPLC water. Argon is then let to bubble through the solution for the period of about 30 minutes. This mixture is then added to the equimolar amount (0.52 g) of isocyanatoethyl methacrylate (IEM, isocyanate titration = 6.45 mEq/g) under stirring. The whole mixture is then stirred under argon flow for 4 hours. The mixture is then filtered through 0.45 μm Teflon filter, degassed with argon in order to remove oxygen and used for photografting.

Example D-8: Preparation of a trehalose macromonomer

55 [0149] 6.45 g of 6-O-carbamoylmethacryloylethyl- α,α' -trehalose telomer with an amino end group (amine titration = 0.12 mEq/g), prepared according to Example D-3 are dissolved in 80 ml of HPLC water. The solution is then degassed by bubbling nitrogen through the solution for 30 minutes. This solution is then added to the equimolar amount (0.12 g) of isocyanatoethyl methacrylate (IEM, isocyanate titration = 6.45 mEq/g) under stirring. The whole mixture is

then stirred under argon flow for 4 hours. The mixture is then filtered through 0.45 µm Teflon filter, degassed with argon in order to remove oxygen and used for photografting.

Synthesis of bottle-brush type coatings on a material surface

5 **Example E-1:** Photografting of an acrylamide macromonomer onto the contact lens surface

[0150] 1 ml of the acrylamide macromonomer solution from Example D-6 is introduced into a small Petri dish of a volume of about 3 ml in a glove box. The dried lens from Example C-1, carrying covalently linked photoinitiator molecules on its surface, is then placed into this solution and an additional 1 ml of the degassed solution is added on the lens in order to cover the whole lens with the solution. After 15 minutes, the Petri dish with the lens in the solution is exposed to 15 mW ultraviolet light for a period of about 3 minutes. The lens is then turned over and the exposition is repeated by applying 15 mW UV light for an additional 3 minutes.

10 The modified lens is then withdrawn from the solution, washed twice in distilled water, continuously extracted in ultra pure water for 16 h and analyzed by ATR-FTIR and contact angle measurements.

15 ATR-FTIR confirms a polyacrylamide-like structure of the coating.

Water/air contact angles on the modified lens are 0° adv., 0° rec., 0° hysteresis. In comparison, the contact angles of non-modified lens are 101° adv., 64° rec., 37° hysteresis.

20 **Example E-2:** Photografting of an acrylamide macromonomer onto the contact lens surface

[0151] Two lenses from Example C-1 are coated in accordance with Example E-1, but instead of 3 minutes of exposition, 2 minutes exposition time are used for photografting.

Water/air contact angles on the modified lenses are 52° adv., 36° rec., 16° hysteresis.

25 **Example E-3:** Photografting of an acryloylmorpholine macromonomer onto the contact lens surface

[0152] 1 ml of the acryloylmorpholine macromonomer solution from Example D-7 are introduced into a small Petri dish of a volume of about 3 ml in a glow box. The dried lens from Example C-1, carrying covalently linked photoinitiator molecules on its surface, is then placed into this solution and an additional 1 ml of the degassed solution are added on the lens in order to cover the whole lens with the solution. After 15 minutes, the Petri dish with the lens in the solution is exposed to 15 mW ultraviolet light for a period of about 3.5 minutes. The lens is then turned over and the exposition is repeated by applying 15 mW UV light for an additional 3.5 minutes.

30 The modified lens is then withdrawn from the solution, washed twice in distilled water, continuously extracted in ultra pure water for 16 h and analyzed by contact angle measurements.

[0153] Water/air contact angles on the modified lens are 67° adv., 39° rec., 28° hysteresis. In comparison, the contact angles of the non-modified lens are 101° adv., 64° rec., 37° hysteresis.

Example E-4: Photografting of a trehalose macromonomer onto the contact lens surface

40 [0154] 1 ml of the trehalose macromonomer solution from Example D-8 is introduced into a small Petri dish of a volume of about 3 ml in a glow box. The dried lens from Example C-1, carrying covalently linked photoinitiator molecules on its surface, is then placed into this solution and an additional 1 ml of the degassed solution are added on the lens in order to cover the whole lens with the solution. After 15 minutes, the Petri dish with the lens in the solution is exposed to 15 mW ultraviolet light for a period of about 3.5 minutes. The lens is then turned over and the exposition is repeated by applying 15 mW UV light for an additional 3.5 minutes.

45 The modified lens is then withdrawn from the solution, washed twice in distilled water, continuously extracted in ultra pure water for 16 h and analyzed by contact angle measurements.

50 Water/air contact angles on the modified lens are 45° adv., 30° rec., 15° hysteresis. In comparison, the contact angles of the non-modified lens are 101° adv., 64° rec., 37° hysteresis.

Example E-5: Photografting of N-vinyl-2-pyrrolidone (NVP) onto the contact lens surface

55 [0155] 2.0 g of NVP are dissolved in 18 ml water and the solution is stirred under argon flow for 5 minutes. Argon is then let to bubble through the solution for the period of about 10 minutes. The solution is then filtered through 0.45 µm Teflon filter and degassed with argon for additional 10 minutes. The filtered solution is then frozen in a flask in liquid nitrogen, the flask evacuated under a high vacuum, transferred into a glove box and used for photografting.

1 ml of the aqueous NVP solution are introduced into a small Petri dish of a volume of about 3 ml in a glove box. The

dried lens from Example C-1, carrying covalently linked photoinitiator molecules on its surface, is then placed into this solution and an additional 1 ml of the degassed solution is added on the lens in order to cover the whole lens with the solution. After 5 minutes, the Petri dish with the lens in the solution is exposed to 15 mW ultraviolet light for a period of about 3 minutes. The lens is then turned over and the exposition is repeated by applying 15 mW UV light for an additional 3 minutes.

The modified lens is then withdrawn from the solution, washed twice in HPLC water, continuously extracted in ultra pure water for 16 h and analyzed by contact angle measurements.

Water/air contact angles on the modified lens are 29° adv., 19° rec., 11° hysteresis. In comparison, the contact angles of non-modified lens are 101° adv., 64° rec., 37° hysteresis.

10

Example E-6: Photografting of an acrylamide macromonomer onto the contact lens surface

[0156] 1 ml of the acrylamide macromonomer solution from Example D-6 is introduced into a small Petri dish of a volume of about 3 ml in a glove box. The dried lens from Example B-6, carrying covalently linked photoinitiator molecules on its surface, is then placed into this solution and an additional 1 ml of the degassed solution is added on the lens in order to cover the whole lens with the solution. After 15 minutes, the Petri dish with the lens in the solution is exposed to 15 mW ultraviolet light for a period of about 3 minutes. The lens is then turned over and the exposition is repeated by applying 15 mW UV light for an additional 3 minutes.

The modified lens is then withdrawn from the solution, washed twice in distilled water, continuously extracted in ultra pure water for 16 h and analyzed by ATR-FTIR and contact angle measurements.

ATR-FTIR confirms a polyacrylamide-like structure of the coating.

Water/air contact angles on the modified lens are 44° adv., 28° rec., 16° hysteresis. In comparison, the contact angles of the non-modified lens are 101° adv., 64° rec., 37° hysteresis.

25 **Example E-7: Photografting of acrylamide monomers (AAm) onto the contact lens surface**

[0157] 2.0 g of AAm are dissolved in 18 ml water and the solution is stirred under argon flow for 5 minutes. Argon is then let to bubble through the solution for the period of about 10 minutes. The solution is then filtered through 0.45 µm Teflon filter and degassed with argon for additional 10 minutes. The filtered solution is then frozen in a flask in liquid nitrogen, the flask is evacuated under a high vacuum, transferred into a glove box and used for photografting.

[0158] 1 ml of the aqueous AAm solution are introduced into a small Petri dish of a volume of about 3 ml in a glove box. The dried lens from Example B-6, carrying covalently linked photoinitiator molecules on its surface, is then placed into this solution and an additional 1 ml of the degassed solution are added on the lens in order to cover the whole lens with the solution. After 5 minutes, the Petri dish with the lens in the solution is exposed to 15 mW ultraviolet light for a period of about 3 minutes. The lens is then turned over and the exposition was repeated by applying 15 mW UV light for an additional 3 minutes.

The modified lens is then withdrawn from the solution, washed twice in HPLC water, continuously extracted in ultra pure water for 16 h and analyzed by contact angle measurements.

Water/air contact angles on the modified lens are 39° adv., 19° rec., 20° hysteresis. In comparison, the contact angles of the non-modified lens are 101° adv., 64° rec., 37° hysteresis.

Claims

1. A process for coating a material surface, comprising the steps of:

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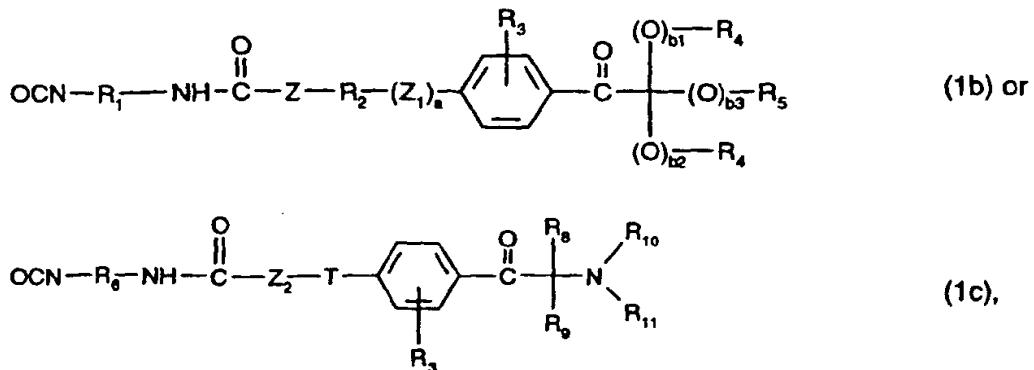
- (a) providing the material surface with polymer brushes comprising polymerization initiator radicals; and
- (b) graft polymerizing one or more different ethylenically unsaturated hydrophilic monomers or macromonomers onto the polymerization initiator-modified polymer brushes.

50 2. A process according to claim 1, wherein the polymer brushes according to step (a) are provided by

- (a1) covalently binding a polymerization initiator to the surface;
- (a2) graft polymerizing a vinyl monomer carrying a reactive group onto the initiator-modified material surface and thereby providing the surface with polymer brushes comprising reactive groups; and
- (a3) reacting the reactive groups of the polymer brushes with a reactive polymerization initiator having a functional group that is coreactive with the reactive groups of the polymer brushes.

3. A process according to claim 1 or 2, wherein in step (a) the surface already comprises or is provided with H-active

groups that are coreactive with isocyanato groups, and said H-active groups are reacted with a polymerization initiator of formula

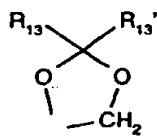


wherein R₁ is branched C₃-C₁₈-alkylene, unsubstituted or C₁-C₄-alkyl- or C₁-C₄-alkoxy-substituted C₆-C₁₀-arylene, or unsubstituted or C₁-C₄-alkyl- or C₁-C₄-alkoxy-substituted C₇-C₁₈-aralkylene, unsubstituted or C₁-C₄-alkyl- or C₁-C₄-alkoxy-substituted C₃-C₈-cycloalkylene, unsubstituted or C₁-C₄-alkyl- or C₁-C₄-alkoxy-substituted C₃-C₈-cycloalkylene-C_yH_{2y}- or unsubstituted or C₁-C₄-alkyl- or C₁-C₄-alkoxy-substituted -C_yH_{2y}-(C₃-C₈-cycloalkylene)-C_yH_{2y}- wherein y is an integer from 1 to 6;

R₂ is a direct bond or linear or branched C₁-C₈-alkylene that is unsubstituted or substituted by -OH and/or is uninterrupted or interrupted by one or more groups -O-, -O-C(O)- or -O-C(O)-O-;

R₃ is H, C₁-C₁₂-alkyl, C₁-C₁₂-alkoxy, N-C₁-C₁₂-alkylamino or N,N-di-C₁-C₁₂-alkylamino;

R₄ and R₅ are each independently of the other H, linear or branched C₁-C₈-alkyl, C₁-C₈-hydroxylalkyl or C₆-C₁₀-aryl, or the groups R₄-(O)_{b1}- and R₄-(O)_{b2}- together are -(CH₂)_c- wherein c is an integer from 3 to 5, or the groups R₄-(O)_{b1}-, R₄-(O)_{b2}- and R₅-(O)_{b3}- together are a radical of the formula



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wherein R₁₃ and R_{13'} are each independently of the other H, C₁-C₈-alkyl, C₃-C₈-cycloalkyl, benzyl or phenyl;

Z is bivalent -O-, -NH- or -NR₁₂-, wherein R₁₂ is linear or branched C₁-C₆-alkyl;

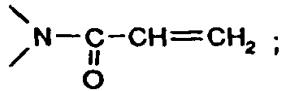
Z₁ is -O-, -O-(O)C-, -C(O)-O- or -O-C(O)-O-;

a, b1, b2 and b3 are each independently of the other 0 or 1;

R₆ independently has the same definitions as R₁ or is linear C₃-C₁₈-alkylene;

Z₂ is a direct bond or -O-(CH₂)_d- wherein d is an integer from 1 to 6 and the terminal CH₂ group of which is linked to the adjacent T in formula (1c);

T is bivalent -O-, -NH-, -S-, C₁-C₈-alkylene or



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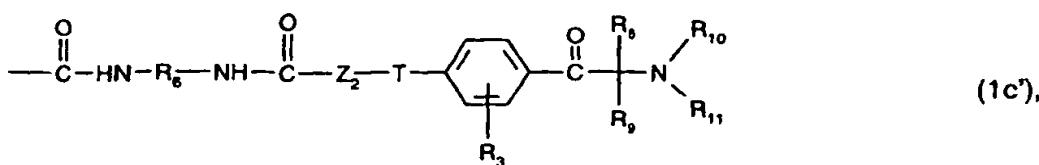
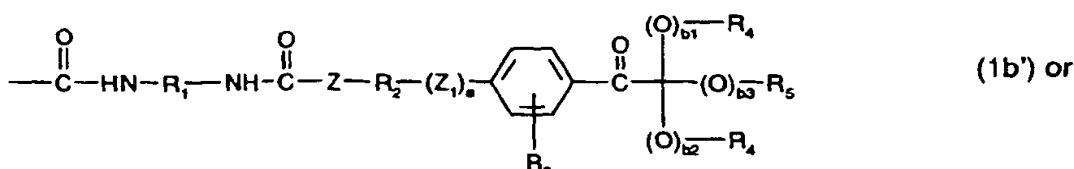
R₈ is linear or branched C₁-C₈-alkyl, C₂-C₈-alkenyl or C₆-C₁₀-aryl-C₁-C₈-alkyl;

55 R₉ independently of R₈ has the same definitions as R₈ or is C₆-C₁₀-aryl, or R₈ and R₉ together are -(CH₂)_e- wherein e is an integer from 2 to 6;

R₁₀ and R₁₁ are each independently of the other linear or branched C₁-C₈-alkyl that may be substituted by C₁-C₄-alkoxy, or C₆-C₁₀-aryl-C₁-C₈-alkyl or C₂-C₈-alkenyl; or R₁₀ and R₁₁ together are -(CH₂)_{f1}-Z₃-(CH₂)_{f2}- wherein Z₃ is a direct bond, -O-, -S- or -NR₇-, and R₇ is H or C₁-C₈-alkyl and f₁ and f₂ are each independently of the other an integer from 2 to 4;

subject to the provisos that b₁ and b₂ are each 0 when R₅ is H; that the total of (b₁+b₂+b₃) is not exceeding 2; and that a is 0 when R₂ is a direct bond.

10 4. A process according to claim 3, wherein the surface is provided with H-active -OH, -NH₂ and/or -NH- groups, in some or all of them an H-atom having been substituted by a radical of formula



25

30 wherein the variables R₁-R₁₁, T, Z, Z₁, Z₂, a, b₁, b₂ and b₃ are as defined in claim 3.

35 5. A process according to any one of claims 2 to 4, wherein the vinyl monomer according to step (a2) is an ethylenically unsaturated compound having from 2 to 18 C-atoms which is substituted by a reactive group selected from the group consisting of a hydroxy, amino, carboxy, carboxylic acid ester, carboxylic acid anhydride, epoxy, lactone, azlactone and isocyanato group.

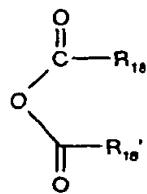
40 6. A process according to any one of claims 2 to 5, wherein the vinyl monomer of step (a2) is of formula



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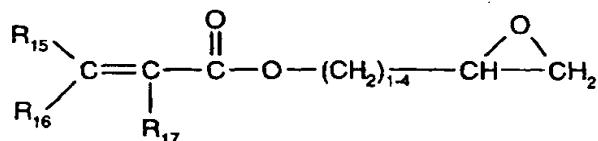
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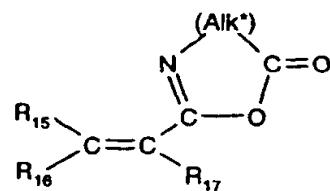
(2b),

10



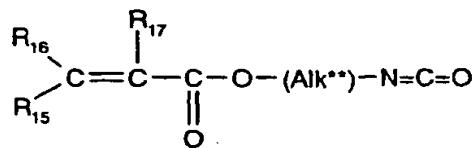
(2c),

15



(2d) or

20



(2e),

25

30

wherein R₁₄ is hydrogen, unsubstituted or hydroxy-substituted C₁-C₆-alkyl or phenyl, R₁₅ and R₁₆ each independently of the other is hydrogen, C₁-C₄-alkyl, phenyl, carboxy or halogen,

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R₁₇ is hydrogen, C₁-C₄-alkyl or halogen,

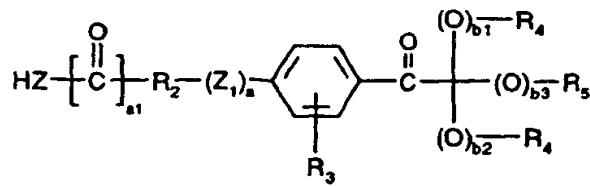
R₁₈ and R_{18'} are each an ethylenically unsaturated radical having from 2 to 6 C-atoms, or

R₁₈ and R_{18'} together form a bivalent radical -C(R₁₅)=C(R₁₇)- wherein R₁₅ and R₁₇ are as defined above, and (Alk') is C₁-C₆-alkylene, and (Alk'') is C₂-C₁₂-alkylene.

40

7. A process according to any one of claims 2 to 6, wherein the reactive polymerization initiator of step (a3) is of formula

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(1a),

50

wherein Z is bivalent -O-, -NH- or -NR₁₂, R₁₂ is linear or branched C₁-C₆-alkyl, a1 is an integer of 0 or 1, and R₂, R₃, R₄, R₅, Z₁, a, b1, b2 and b3 are each independently defined as in claim 3.

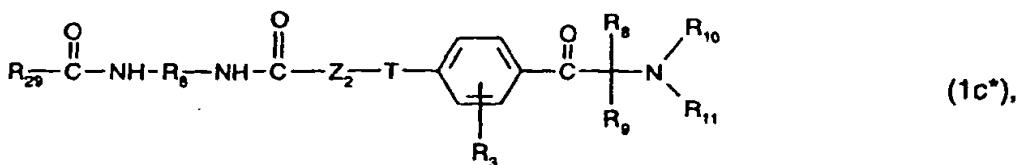
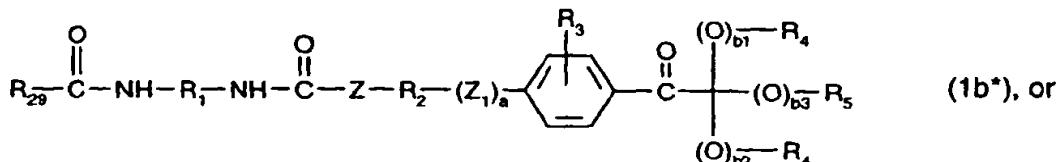
8. A process according to claim 1, wherein the polymer brushes according to step (a) of the process are provided by

(a1) covalently binding a polymerization initiator to the surface; and

(a2') graft polymerizing an ethylenically unsaturated polymerization initiator onto the initiator-modified material surface, wherein said ethylenically unsaturated polymerization initiator is a photoinitiator in case of a thermal polymerization initiator in step (a1), or is a thermal polymerization initiator in case of a photoinitiator in step (a1).

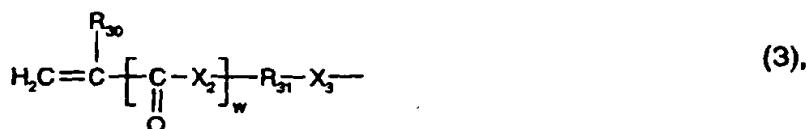
9. A process according to claim 8, wherein the polymerization initiator of step (a1) is a thermal polymerization initiator, preferably an azo-bis(C₂-C₁₂-alkane carboxylic acid) wherein the alkane moiety is in each case unsubstituted or substituted by cyano.

10. A process according to claim 8 or 9, wherein the ethylenically unsaturated polymerization initiator of step (a2') is of formula



30

wherein R₁, R₂, R₃, R₄, R₅, R₆, R₈, R₉, R₁₀, R₁₁, T, Z, Z₁, Z₂, b1, b2 and b3 are each independently as defined in claim 3, and R₂₉ is a radical of formula



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wherein R₃₀ is hydrogen or methyl, R₃₁ is C₁-C₁₂-alkylene, C₁-C₆-alkylenephenoxy or phenoxy-C₁-C₆-alkylene, or if w is 0 may also be a direct bond, w is 0 or 1, and X₂ and X₃ are each independently of the other -O- or -NH-.

45

11. A process according to any one of claim 1 to 10, wherein in step (b) a hydrophilic monomer is graft polymerized onto the polymerization initiator-modified polymer brushes, and wherein the hydrophilic monomer is selected from the group consisting of hydroxy-substituted C₁-C₄-alkyl acrylates and methacrylates, acrylamide, methacrylamide, mono- and di-C₁-C₄ alkylacrylamides and -methacrylamides, ethoxylated acrylates and methacrylates, hydroxy-substituted C₁-C₄-alkylacrylamides and methacrylamides, hydroxy-substituted C₁-C₄-alkyl vinyl ethers, sodium ethylenesulfonate, sodium styrenesulfonate, 2-acrylamido-2-methylpropanesulfonic acid, N-vinylpyrrole, N-vinylsuccinimide, N-vinylpyrrolidone, 2- and 4-vinylpyridine, vinylically unsaturated carboxylic acids having a total of from 3 to 5 carbon atoms, amino-, mono-C₁-C₄-alkylamino- or di-C₁-C₄-alkylamino-C₁-C₄-alkyl acrylates and methacrylates, vinylacetate and allyl alcohol.

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12. A process according to any one of claim 1 to 10, wherein in step (b) a macromonomer of formula



is graft polymerized onto the polymerization initiator-modified polymer brushes,

10 wherein R₃₂ is hydrogen, C₁-C₆-alkyl or a radical -COOR';
 R, R' and R₃₂' are each independently of the other hydrogen or C₁-C₆-alkyl;
 A is a direct bond or is a radical of formula

15 $-\text{C}(\text{O})-(\text{A}_1)_n-\text{X}-$ (5a)

or

20 $-(\text{A}_2)_m-\text{NH}-\text{C}(\text{O})-\text{X}-$ (5b);

or

25 $-(\text{A}_2)_m-\text{X}-\text{C}(\text{O})-$ (5c);

or

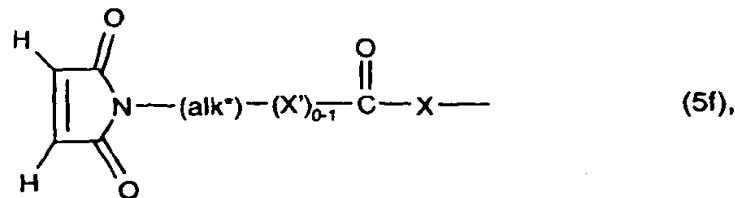
30 $-\text{C}(\text{O})-\text{NH}-\text{C}(\text{O})-\text{X}-$ (5d);

or

35 $-\text{C}(\text{O})-\text{X}_1-(\text{alk}^*)-\text{X}-\text{C}(\text{O})-$ (5e);

or

35 A and R₃₂, together with the adjacent double bond, are a radical of formula



45 A₁ is -O-C₂-C₁₂-alkylene which is unsubstituted or substituted by hydroxy, or is -O-C₂-C₁₂-alkylene-NH-C(O)- or -O-C₂-C₁₂-alkylene-O-C(O)-NH-R₃₃-NH-C(O)- or -NH-(Alk^{*})-C(O), wherein (Alk^{*}) is C₁-C₆-alkylene and

50 R₃₃ is linear or branched C₁-C₁₈-alkylene or unsubstituted or C₁-C₄-alkyl- or C₁-C₄-alkoxy-substituted C₆-C₁₀-arylene, C₇-C₁₈-aralkylene, C₆-C₁₀-arylene-C₁-C₂-alkylene-C₆-C₁₀-arylene, C₃-C₈-cycloalkylene, C₃-C₈-cycloalkylene-C₁-C₆-alkylene, C₃-C₈-cycloalkylene-C₁-C₂-alkylene-C₃-C₈-cycloalkylene or C₁-C₆-alkylene-C₃-C₈-cycloalkylene-C₁-C₆-alkylene;

55 A₂ is C₁-C₈-alkylene; phenylene or benzylene;

or m and n are each independently of the other the number 0 or 1;

X, X₁ and X' are each independently of the other a bivalent group -O- or -NR", wherein R" is hydrogen or C₁-C₆-alkyl;

(alk^{*}) is C₂-C₁₂-alkylene;

and (oligomer) denotes

(i) the radical of a telomer of formula

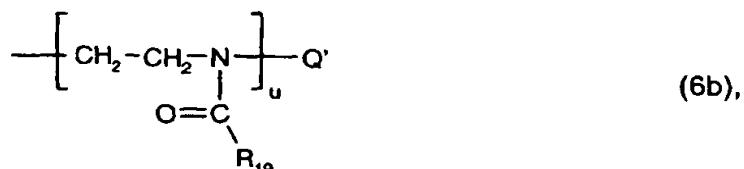


5

wherein (alk) is $\text{C}_2\text{-C}_{12}$ -alkylene,

10 Q is a monovalent group that is suitable to act as a polymerization chain-reaction terminator,
 p and q are each independently of another an integer from 0 to 350, wherein the total of (p+q) is an
 integer from 2 to 350,
 and B and B' are each independently of the other a 1,2-ethylene radical derivable from a copolymer-
 15 izable vinyl monomer by replacing the vinylic double bond by a single bond, at least one of the radicals
 B and B' being substituted by a hydrophilic substituent; or

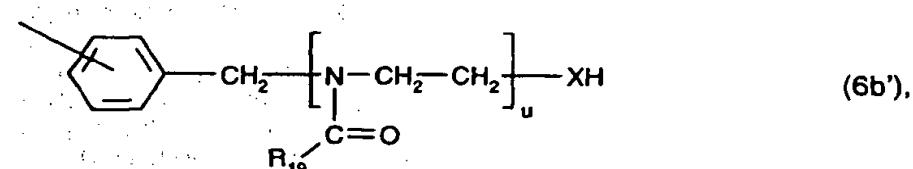
(ii) the radical of an oligomer of the formula



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wherein R_{19} is hydrogen or unsubstituted or hydroxy-substituted $\text{C}_1\text{-C}_{12}$ -alkyl, u is an integer from 2
 30 to 250 and Q' is a radical of a polymerization initiator; or

(iii) the radical of formula

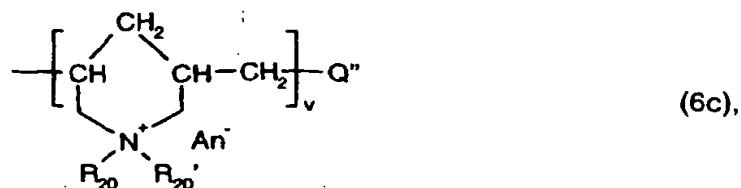


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wherein R_{19} , X and u are as defined above, or

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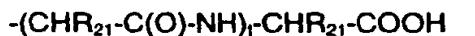
(iv) the radical of an oligomer of formula



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wherein R_{20} and R_{20}' are each independently C_1 - C_4 -alkyl, An^- is an anion, v is an integer from 2 to 250, and Q'' is a monovalent group that is suitable to act as a polymerization chain-reaction terminator; or

5 (v) the radical of an oligopeptide of formula



(6d) or

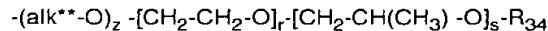


(6d'),

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15 wherein R_{21} is hydrogen or C_1 - C_4 -alkyl which is unsubstituted or substituted by hydroxy, carboxy, carbamoyl, amino, phenyl, o-, m- or p-hydroxyphenyl, imidazolyl, indolyl or a radical $-NH-C(=NH)-NH_2$ and t is an integer from 2 to 250, or the radical of an oligopeptide based on proline or hydroxyproline; or

20 (vi) the radical of a polyalkylene oxide of formula



(6e),

25 wherein R_{34} is hydrogen or C_1 - C_{24} -alkyl, (alk^{**}) is C_2 - C_4 -alkylene, z is 0 or 1, r and s are each independently an integer from 0 to 250 and the total of $(r+s)$ is from 2 to 250; or

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(vii) the radical of an oligosaccharide,
subject to the provisos that

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A is not a direct bond if (oligomer) is a radical of formula (6a);

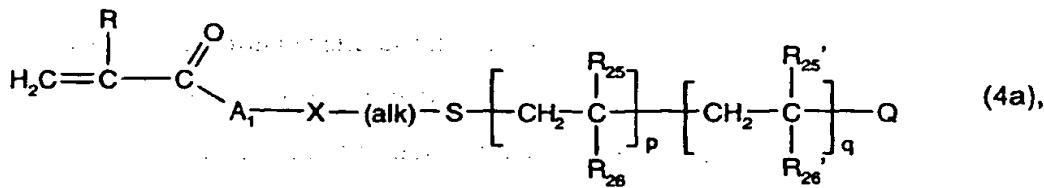
A is a radical of formula (5a), (5b) or (5d) or A and R_{32} , together with the adjacent double bond, are a radical of formula (5f) if (oligomer) is a radical of formula (6b), (6c), (6d) or (6e) or is the radical of an oligosaccharide;

A is a direct bond if (oligomer) is a radical of formula (6b'); and

A is a radical of formula (5c) or (5e) if (oligomer) is a radical of formula (6d')

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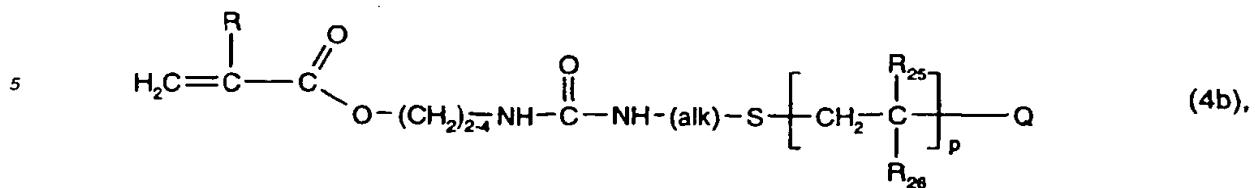
13. A process according to claim 12, wherein the macromonomer is of formula



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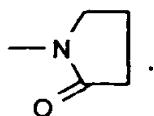
wherein R is hydrogen or methyl, A_1 is $-O-(CH_2)_{2-4}-$, $-O-CH_2-CH(OH)-CH_2-$ or a radical $-O-(CH_2)_{2-4}-NH-C(O)-$, X is $-O-$ or $-NH-$, (alk) is C_2 - C_4 -alkylene, Q is a monovalent group that is suitable to act as a polymerization chain-reaction terminator, p is an integer from 5 to 50, R_{25} and R_{25}' are each independently of the other hydrogen or methyl, and R_{26} and R_{26}' are each independently a radical $-COOY$, wherein Y is C_1 - C_2 -alkyl, C_2 - C_3 -alkyl, which is substituted by hydroxy, amino or N,N-di- C_1 - C_2 -alkylamino, or is a radical $-C_2$ - C_4 -alkylene- $NH-C(O)-O-G$ wherein $-O-G$ is the radical of trehalose or a cyclodextrin fragment with a maximum of 8 sugar units; or a radical $-CO-NY_1Y_2$, wherein Y_1 and Y_2 are each independently of the other hydrogen or C_1 - C_4 -alkyl which is unsubstituted or substituted by hydroxy, or Y_1 and Y_2 together with the adjacent N-atom form a N- C_1 - C_2 -alkylpiperazino or morpholino ring; or a heterocyclic radical selected from the group consisting of N-pyrrolidonyl, 2- or 4-pyridinyl, 2-methylpyridin-5-yl, 2-, 3- oder 4-hydroxypyridinyl, N- ϵ -caprolactamyl, N-imidazolyl, 2-methylimidazol-1-yl, N-morpholinyl and 4-N-methylpiperazin-1-yl.

14. A process according to claim 12, wherein the macromonomer is of formula



wherein R is hydrogen or methyl, (alk) is C₂-C₄-alkylene, R₂₅ is hydrogen or methyl, p is an integer of 5 to 50, Q is as defined in claim 12, and R₂₆ is a radical -CONH₂, -CON(CH₃)₂ or

15



25 15. A coated material that is obtainable by the process of any one of claims 1 to 14.

16. A coated material according to claim 15, which is a biomedical device, preferably an ophthalmic device, in particular a contact lens, intraocular lens or artificial cornea.

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(19)



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(71) Applicants:

• Novartis AG
4056 Basel (CH)

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• Novartis-Erfindungen Verwaltungsgesellschaft
m.b.H.
1230 Wien (AT)

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(72) Inventors:

- Chabrecek, Peter
4125 Riehen (CH)
- Lohmann, Dieter
4141 Münchenstein (CH)

(74) Representative: Becker, Konrad

Novartis AG,
Corporate Intellectual Property,
Patent & Trademark Department
4002 Basel (CH)

(54) Process for coating a material surface

(57) The invention relates to a process for coating a material surface, comprising the steps:

- providing the material surface with polymer brushes comprising polymerization initiator radicals; and
- graft polymerizing one or more different ethylenically unsaturated hydrophilic monomers or macromonomers onto the polymerization initiator-mod-

ified polymer brushes.

The coated articles that are obtainable by the process of the invention have desirable characteristics regarding adherence to the substrate, durability, hydrophilicity, wettability, biocompatibility and permeability and are thus useful for the manufacture of biomedical articles such as ophthalmic devices.



DOCUMENTS CONSIDERED TO BE RELEVANT																		
Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	CLASSIFICATION OF THE APPLICATION (Int.Cl.7)															
P, X	WO 99 57581 A (NOVARTIS ERFIND VERWALT GMBH ; NOVARTIS AG (CH); CHABRECEK PETER (C) 11 November 1999 (1999-11-11) * claims; examples *	1,3,6-8, 10-16	B05D7/00 B05D1/18															
X	EP 0 632 329 A (CIBA GEIGY AG) 4 January 1995 (1995-01-04) * claims 1,52-56; examples *	1-3,6, 12-16																
D, X	& US 5 527 925 A (CHABRECEK ET AL.) 18 June 1996 (1996-06-18)	1-3,6, 12-16																
X	WO 96 20796 A (CIBA GEIGY AG ; CHABRECEK PETER (CH); LOHmann DIETER (CH)) 11 July 1996 (1996-07-11) * claims; examples *	1,3																
X	WO 99 15917 A (NOVARTIS ERFIND VERWALT GMBH ; NOVARTIS AG (CH)) 1 April 1999 (1999-04-01) * claims; examples *	1																
X	US 5 071 732 A (GREBER GERHARD ET AL) 10 December 1991 (1991-12-10) * claims; examples *	1	TECHNICAL FIELDS SEARCHED (Int.Cl.7) B05D C08J G02B															
X	WO 96 20919 A (CIBA GEIGY AG ; CHABRECEK PETER (CH); DIETLIKER KURT (CH); LOHmann) 11 July 1996 (1996-07-11) * claims; examples *	1																
<p>The present search report has been drawn up for all claims</p> <table border="1" style="width: 100%; border-collapse: collapse;"> <tr> <td style="width: 33%;">Place of search:</td> <td style="width: 33%;">Date of completion of the search</td> <td style="width: 34%;">Examiner</td> </tr> <tr> <td>THE HAGUE</td> <td>28 September 2001</td> <td>Slembrouck, I</td> </tr> <tr> <td colspan="3">CATEGORY OF CITED DOCUMENTS</td> </tr> <tr> <td colspan="3"> X: particularly relevant if taken alone Y: particularly relevant if combined with another document of the same category A: technological background O: non-written disclosure P: intermediate document </td> </tr> <tr> <td colspan="3"> T: theory or principle underlying the invention E: earlier patent document, but published on, or after the filing date D: document cited in the application L: document cited for other reasons & : member of the same patent family, corresponding document </td> </tr> </table>				Place of search:	Date of completion of the search	Examiner	THE HAGUE	28 September 2001	Slembrouck, I	CATEGORY OF CITED DOCUMENTS			X: particularly relevant if taken alone Y: particularly relevant if combined with another document of the same category A: technological background O: non-written disclosure P: intermediate document			T: theory or principle underlying the invention E: earlier patent document, but published on, or after the filing date D: document cited in the application L: document cited for other reasons & : member of the same patent family, corresponding document		
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This annex lists the patent family members relating to the patent documents cited in the above-mentioned European search report. The members are as contained in the European Patent Office EDP file on. The European Patent Office is in no way liable for these particulars which are merely given for the purpose of information.

28-09-2001

Patent document cited in search report		Publication date		Patent family member(s)	Publication date
WO 9957581	A	11-11-1999	AU BR CN WO EP NO	3824899 A 9910056 A 1298489 T 9957581 A1 1084428 A1 20005446 A	23-11-1999 09-01-2001 06-06-2001 11-11-1999 21-03-2001 27-10-2000
EP 0632329	A	04-01-1995	AT AU AU CA CN CZ DE DK EP ES FI GR HK HU IL JP MX NO NZ PL US US US US ZA	160888 T 683256 B2 6603994 A 2127200 A1 1102825 A 9401610 A3 59404708 D1 632329 T3 0632329 A1 2109647 T3 943129 A 3025768 T3 1003846 A1 69305 A2 110171 A 7089925 A 9404973 A1 942495 A 260892 A 304064 A1 5527925 A 5612389 A 5612391 A 5621018 A 9404758 A	15-12-1997 06-11-1997 23-02-1995 03-01-1995 24-05-1995 18-01-1995 15-01-1998 04-05-1998 04-01-1995 16-01-1998 03-01-1995 31-03-1998 06-11-1998 28-09-1995 11-04-1999 04-04-1995 31-01-1995 03-01-1995 27-02-1996 09-01-1995 18-06-1996 18-03-1997 18-03-1997 15-04-1997 03-01-1995
WO 9620796	A	11-07-1996	AT AT AT AT AU AU AU AU AU AU AU AU AU AU AU AU AU AU AU AU AU AU AU	176915 T 173742 T 184812 T 180185 T 4251496 A 692979 B2 4251596 A 701751 B2 4251696 A 698098 B2 4387496 A 9510122 A 9510292 A	15-03-1999 15-12-1998 15-10-1999 15-06-1999 24-07-1996 18-06-1998 24-07-1996 04-02-1999 24-07-1996 22-10-1998 24-07-1996 30-12-1997 11-11-1997

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ANNEX TO THE EUROPEAN SEARCH REPORT
ON EUROPEAN PATENT APPLICATION NO.

EP 00 12 3172

This annex lists the patent family members relating to the patent documents cited in the above-mentioned European search report. The members are as contained in the European Patent Office EDP file on. The European Patent Office is in no way liable for these particulars which are merely given for the purpose of information.

28-09-2001

Patent document cited in search report		Publication date	Patent family member(s)	Publication date	
WO 9620796	A		BR 9510415 A BR 9510434 A CA 2208710 A1 CA 2208967 A1 CA 2208977 A1 CA 2208996 A1 WO 9620964 A1 WO 9621167 A1 WO 9620795 A1 CN 1171798 A CN 1173227 A CN 1173148 A CN 1174525 A CZ 9702061 A3 DE 59504366 D1 DE 59505153 D1 DE 59506915 D1 DE 69509801 D1 DE 69509801 T2 DK 800657 T3 DK 793541 T3 DK 808222 T3 WO 9620796 A1 EP 0800541 A1 EP 0800657 A1 EP 0793541 A1 EP 0808222 A1 ES 2128110 T3 ES 2125676 T3 ES 2138246 T3 ES 2134514 T3 FI 972611 A FI 972699 A FI 9727 A	19-05-1998 13-10-1999 11-07-1996 11-07-1996 11-07-1996 11-07-1996 11-07-1996 11-07-1996 28-01-1998 11-02-1998 11-02-1998 25-02-1998 15-10-1997 07-01-1999 01-04-1999 28-10-1999 24-06-1999 14-10-1999 09-08-1999 10-04-2000 29-11-1999 11-07-1996 15-10-1997 15-10-1997 10-09-1997 26-11-1997 01-05-1999 01-03-1999 01-01-2000 01-10-1999 18-06-1997 22-08-1997	
WO 9915917	A	01-04-1999	AU 9627298 A WO 9915917 A1 EP 1023617 A1 ZA 9808670 A	12-04-1999 01-04-1999 02-08-2000 23-03-1999	
US 5071732	A	10-12-1991	DE 3702897 A1 AU 600746 B2 AU 7749287 A BR 8704460 A CS 8706239 A2 DK 453587 A	11-08-1988 23-08-1990 03-03-1988 19-04-1988 12-03-1991 01-03-1988	

For more details about this annex : see Official Journal of the European Patent Office, No. 12/82

ANNEX TO THE EUROPEAN SEARCH REPORT
ON EUROPEAN PATENT APPLICATION NO.

EP 00 12 3172

This annex lists the patent family members relating to the patent documents cited in the above-mentioned European search report. The members are as contained in the European Patent Office EPO file on. The European Patent Office is in no way liable for these particulars which are merely given for the purpose of information.

28-09-2001

Patent document cited in search report		Publication date		Patent family member(s)	Publication date
US 5071732	A			EP 0258719 A2	09-03-1988
				FI 873755 A	01-03-1988
				JP 63063030 A	19-03-1988
				US 4914004 A	03-04-1990
				ZA 8706457 A	27-04-1988
WO 9620919	A	11-07-1996		AT 176915 T	15-03-1999
				AT 173742 T	15-12-1998
				AT 184812 T	15-10-1999
				AT 189210 T	15-02-2000
				AU 4251496 A	24-07-1996
				AU 692979 B2	18-06-1998
				AU 4251596 A	24-07-1996
				AU 701751 B2	04-02-1999
				AU 4251696 A	24-07-1996
				AU 700575 B2	07-01-1999
				AU 4387396 A	24-07-1996
				BR 9510122 A	30-12-1997
				BR 9510177 A	23-12-1997
				BR 9510434 A	13-10-1999
				CA 2208664 A1	11-07-1996
				CA 2208967 A1	11-07-1996
				CA 2208977 A1	11-07-1996
				CA 2208996 A1	11-07-1996
				WO 9620964 A1	11-07-1996
				WO 9621167 A1	11-07-1996
				WO 9620795 A1	11-07-1996
				CN 1171798 A	28-01-1998
				CN 1173227 A	11-02-1998
				CN 1173148 A	11-02-1998
				CN 1174547 A	25-02-1998
				CZ 9702061 A3	15-10-1997
				DE 59504366 D1	07-01-1999
				DE 59505153 D1	01-04-1999
				DE 59506915 D1	28-10-1999
				DE 69514835 D1	02-03-2000
				DE 69514835 T2	17-08-2000
				DK 800657 T3	09-08-1999
				DK 793541 T3	10-04-2000
				DK 800511 T3	19-06-2000
				WO 9620919 A1	11-07-1996
				EP 0800541 A1	15-10-1997
				EP 0800657 A1	15-10-1997
				EP 0793541 A1	10-09-1997
				EP 0800511 A1	15-10-1997
				ES 2128110 T3	01-05-1999

ANNEX TO THE EUROPEAN SEARCH REPORT
ON EUROPEAN PATENT APPLICATION NO.

EP 00 12 3172

This annex lists the patent family members relating to the patent documents cited in the above-mentioned European search report. The members are as contained in the European Patent Office EDP file on The European Patent Office is in no way liable for these particulars which are merely given for the purpose of information.

28-09-2001

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 9620919 A		ES 2125676 T3	01-03-1999
		ES 2138246 T3	01-01-2000
		ES 2142506 T3	16-04-2000
		FI 972611 A	18-06-1997
		FI 972698 A	25-08-1997
		FI 972737 A	27-08-1997
		FI 9727 A	

EPO-00123172-0459

For more details about this annex : see Official Journal of the European Patent Office, No. 12/82